American Heart Journal

VOL. 33 | MAY, 1947 | NO. 5

Inter-American Number

As a recognition of its importance and as a contribution to its full success, the American Heart Association and the Editorial Board and publishers of its official JOURNAL are devoting this entire issue of the AMERICAN HEART JOURNAL to the transactions of the Second Inter-American Congress of Cardiology, which was held in Mexico City in October, 1946.

This issue has been made a large one in order that as many papers as possible might be published in full. Some contributions have appeared in earlier issues and some additional ones will appear in subsequent issues. The Board regrets exceedingly that it cannot publish every paper in full and that so many excellent papers must appear in an abbreviated form.

THE SECOND INTER-AMERICAN CONGRESS OF CARDIOLOGY AND THE FORMATION OF THE INTER-AMERICAN SOCIETY OF CARDIOLOGY

The second Inter-American Congress of Cardiology convened in Mexico City on Oct. 6, 1946, under the direction of its President, Professor Ignacio Chávez. The scientific sessions were held at the National Institute of Cardiology of Mexico, of which Dr. Chávez is the Director.

The sponsoring societies and institutions were as follows:

Sociedad Interamericana de Cardiología
The American Heart Association
Sociedad Argentina de Cardiología
Sociedade Brasileira de Cardiologia
Sociedad Cubana de Cardiología
Instituto Nacional de Cardiología de México
Secretaría de Salubridad y Asistencia Pública de México
Secretaría de Relaciones Exteriores de México
Universidad Nacional Autónoma de México

American Heart Association, Inc.

1790 Broadway, New York 19, N. Y.

Telephone Circle 5-8000

OFFICERS

Vice-President	*President*	*Secretary*
Dr. Arlie R. Barnes	Dr. Howard F. West	Dr. Howard B. Sprague
Treasurer	*Acting Executive Secretary*	*Acting Medical Director*
Dr. George R. Herrmann	Dr. H. M. Marvin	Dr. David D. Rutstein

DIRECTORS

Dr. Edgar V. Allen............Rochester, Minn.
Dr. Graham Asher............Kansas City, Mo.
*Dr. Arlie R. Barnes............Rochester, Minn.
Dr. Alfred Blalock............Baltimore
*Dr. William H. Bunn............Youngstown, Ohio
Dr. Clarence de la Chapelle............New York City
*Dr. Tinsley R. Harrison............Dallas
Dr. George R. Herrmann............Galveston
Dr. T. Duckett Jones............Boston
Dr. Louis N. Katz............Chicago
Dr. Samuel A. Levine............Boston
Dr. Gilbert Marquardt............Chicago
*Dr. H. M. Marvin............New Haven
*Dr. Edwin P. Maynard, Jr............Brooklyn
*Dr. Thomas M. McMillan............Philadelphia
Dr. Jonathan Meakins............Montreal, Can.
Dr. E. Sterling Nichol............Miami

*Executive Committee.

Dr. Harold E. B. Pardee............New York City
Dr. William B. Porter............Richmond, Va.
*Dr. David D. Rutstein............New York City
*Dr. John J. Sampson............San Francisco
Dr. Roy W. Scott............Cleveland
*Dr. Howard B. Sprague............Boston
Dr. George F. Strong............Vancouver, B. C., Can.
Dr. William D. Stroud............Philadelphia
Dr. Homer F. Swift............New York City
Dr. William P. Thompson............Los Angeles
Dr. Harry E. Ungerleider............New York City
*Dr. Howard F. West............Los Angeles
Dr. Paul D. White............Boston
Dr. Frank N. Wilson............Ann Arbor
*Dr. Irving S. Wright............New York City
Dr. Wallace M. Yater............Washington, D. C.

THE American Heart Association was founded in 1924 "for the study of and the dissemination and application of knowledge concerning the causes, treatment and prevention of heart disease; the gathering of information on heart disease; the development and application of measures that would prevent heart disease; seeking and provision of occupations suitable for heart disease patients; the promotion of the establishment of special dispensary classes for heart disease patients; the extension of opportunities for adequate care of cardiac convalescents; the promotion of permanent institutional care for such cardiac patients as are hopelessly incapacitated from self-support; and the encouragement and establishment of local associations with similar objects throughout the United States."

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The American Council on Rheumatic Fever, organized in 1944, consists of a group of representatives of all national medical organizations concerned with rheumatic fever. It operates administratively through the American Heart Association and carries out the program of the American Heart Association insofar as that relates to rheumatic fever.

Annual membership in the American Heart Association is $2.50 and includes twelve issues of *Modern Concepts of Cardiovascular Disease;* Journal membership is $10.00 and includes a year's subscription to the American Heart Journal (January-December), twelve issues of *Modern Concepts of Cardiovascular Disease*, and annual membership in the Association. Contributing membership starts at $25.00 per year; patron membership is $50.00 and over per year. Membership blanks will be sent upon request.

The Association earnestly solicits your support and suggestions for its work. Donations will be gratefully received and promptly acknowledged.

Annual Meeting

The Annual Meeting and Twentieth Scientific Sessions of the American Heart Association will be held in Atlantic City, N. J., June 6 and 7, 1947. The Hotel President will be the headquarters for all meetings. On June 6, a meeting will be held with representatives of local Heart Associations to discuss the administrative structure of the American Heart Association with particular reference to program. The annual meeting of members will also be held on that day. The scientific sessions will take place on June 6 and 7. The annual dinner is scheduled for Saturday evening, June 7, at the Hotel President. Meetings begin at 9:00 A.M. each day, and members should plan to arrive on June 5. Hotel rooms will be in great demand and every member who wishes to attend is urged to make reservations immediately.

The chairman of the Program Committee for the Annual Scientific Sessions of the American Heart Association is Dr. Edgar V. Allen, Mayo Clinic, Rochester, Minn. All who desire to present papers at the meetings of June 6 and 7 in Atlantic City should forward to him an abstract of the proposed presentation of not more than 300 words. The deadline for the receipt of abstracts is March 30, 1947.

American Heart Journal

VOL. 33 MAY, 1947 No. 5

Inter-American Number

As a recognition of its importance and as a contribution to its full success, the American Heart Association and the Editorial Board and publishers of its official JOURNAL are devoting this entire issue of the AMERICAN HEART JOURNAL to the transactions of the Second Inter-American Congress of Cardiology, which was held in Mexico City in October, 1946.

This issue has been made a large one in order that as many papers as possible might be published in full. Some contributions have appeared in earlier issues and some additional ones will appear in subsequent issues. The Board regrets exceedingly that it cannot publish every paper in full and that so many excellent papers must appear in an abbreviated form.

THE SECOND INTER-AMERICAN CONGRESS OF CARDIOLOGY AND THE FORMATION OF THE INTER-AMERICAN SOCIETY OF CARDIOLOGY

The second Inter-American Congress of Cardiology convened in Mexico City on Oct. 6, 1946, under the direction of its President, Professor Ignacio Chávez. The scientific sessions were held at the National Institute of Cardiology of Mexico, of which Dr. Chávez is the Director.

The sponsoring societies and institutions were as follows:

Sociedad Interamericana de Cardiología
The American Heart Association
Sociedad Argentina de Cardiología
Sociedade Brasileira de Cardiologia
Sociedad Cubana de Cardiología
Instituto Nacional de Cardiología de México
Secretaría de Salubridad y Asistencia Pública de México
Secretaría de Relaciones Exteriores de México
Universidad Nacional Autónoma de México

The Board of Directors and Honorary Members included leading officials of the Republic of Mexico headed by President Avila Camacho.

Honorary guests of the Congress were the following:

Dr. Joseph Brumlik, Profesor de la Universidad de Praga (Czechoslovakia)
Dr. Pierre Duchosal, Médico Adjunto del Hospital Universitario de Ginebra (Switzerland)
Dr. Gaston Giraud, Decano de la Facultad de Medicina de Montpellier (France)
Dr. Charles Laubry, Presidente de la Sociedad Francesa de Cardiología, Miembro de la Academia (France)
Dr. Jean Lequime, Delegado de la Sociedad Belga de Cardiología (Belgium)
Dr. Ivan Mahaim, Profesor de la Universidad de Lausanne (Switzerland)
Dr. Gustav Nylin, Profesor de Clínica Médica en el Sabbatsbergs Sjukhus de Estocolmo (Sweden)
Dr. V. Puddu, Director del Centro para la Lucha contra el Reumatismo y las Cardiopatías, del Policlínico de Roma (Italy)
Dr. Daniel Routier, Delegado de la Sociedad Francesa de Cardiología (France)
Dr. J. Snellen, Delegado de la Sociedad Holandesa de Cardiología (Holland)
Dr. Eric Warburg, Profesor de Medicina Internaen el Rigshospitalet de Copenhague (Denmark)

The session opened at the Bolívar Amphitheatre of the University on Sunday, October 6, and the scientific meetings continued daily through the week at the National Institute of Cardiology where the members had an opportunity to see a building and equipment dedicated to the study of cardiovascular disease which are unique in the history of cardiology.

On hundred eleven papers were on the program for the four and one-half days. They were delivered in Spanish, English, French, and Portuguese. Abstracts in English or Spanish were available at each meeting for members unable to understand the language of the one delivering the address, and in the larger meetings Spanish- and English-speaking members were available to translate the discussions orally for the audience.

The social diversions to which the members were invited were splendidly organized and lavish. These included a luncheon at Montezuma's ancient palace of Chapultapec, a banquet with a demonstration of Mexican folklore and art, a luncheon and visit to the pyramids of San Juan Teotihuacán, and a reception and ball at the palace of the Secretary of Foreign Relations.

On October 11 a business meeting was held at which a permanent Inter-American Society of Cardiology was formed and a constitution adopted. Dr. Ignacio Chávez was elected Honorary President for life and the National Institute of Cardiology of Mexico designated the permanent secretariat. This Society is to be under a Council of Directors of which five represent South and Central America and five North America. The Directors from the South are

Dr. Rámon Aixalá (Cuba), Dr. Herman Alessandri (Chile), Dr. Eduardo Braun Menéndez (Argentina), Dr. Teófilo Ortiz Ramírez (Mexico), and Dr. Jairo Ramos (Brazil). Those from the North are Dr. Arlie Barnes (Rochester, Minn.), Dr. George R. Herrmann (Galveston, Texas), Dr. William Kerr (San Francisco, Calif.), Dr. Howard B. Sprague (Boston, Mass.), and Dr. John Hepburn (Toronto, Ontario, Can.).

The constitution was signed by Dr. Teófilo Ortiz Ramírez, Dr. Rodolfo Pérez de los Reyes, Dr. Howard F. West, Dr. Francisco Laranja, Dr. Luis V. Decourt, and Dr. Alberto C. Taquini for the Cardiac Societies of the countries of Mexico, Cuba, United States, Brazil, and Argentina.

The Society plans to meet every two years, the next time in 1948 in the United States. At the time of organization of the Society an International Council was also appointed to arrange an international Congress every six years.

The formation of this Inter-American Society of Cardiology and of the International Council is an important step in the history of the cooperative study of cardiovascular disease. Science is without boundaries, but individuals are nationalistic. The members of the Second International Congress know from their delightful and stimulating experience in Mexico that this interchange of social and medical ideas will be of benefit to both sides of the Rio Grande.

DIRECT INTRACARDIAC ANGIOCARDIOGRAPHY—ITS DIAGNOSTIC VALUE

IGNACIO CHÁVEZ, M.D.,* NARNO DORBECKER, M.D.,* AND ALEJANDRO CELIS, M.D.†

MEXICO, D. F., MEXICO

USING the Forssmann[1,2] technique of heart catheterization, Egaz Monis, Lopo Carvalho, and Alen Saldana[5] injected concentrated solution of iodide through the catheter and with x-ray exposures at the end of the injection obtained beautiful images of the great vessels. They called their method *pneumo-angiography* and in 1931, applied this method to the study of the great vessels in tuberculous patients.

In 1937 Castellanos and co-workers[6-8] published a method by which visualization of the heart chambers could be obtained in living persons. The method consists of rapid injection of radiopaque substance (35 or 50 per cent Per-Abrodil or uroselectan) into the venous blood stream through the antecubital veins, the amount injected varying from 10 to 15 c.c. according to the child's age. Films should be overexposed. This method, angiocardiography, is very useful and has made possible the diagnosis of many congenital heart anomalies.

A year later, in 1938, Robb and Steinberg[9] applied the method to adults. It was necessary to modify the amount and the concentration of the dye, the average amount used being 30 to 40 c.c. of a 70 per cent solution. In addition, by determining the circulatory time (T.C.S.) and filming the right and left chambers at the proper moments, they obtained for the first time the image of the left chambers and the aorta. Unfortunately, the high opacity obtained by Castellanos in children could not be attained in adults. Nevertheless, in some fortunate cases, Robb, Steinberg, Sussman, Taylor, and McGovern and associates[9,11-15] have been able to obtain good diagnostic films of the left atrium in mitral rheumatic heart disease and of the aorta and aortic aneurisms.‡

Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

*National Institute of Cardiology.

†General Hospital.

‡After the reading of this paper we received a communication from Dr. Pérez Ara[3] of Cuba and the reprint of his paper, "Right Heart Catheterisation," published in July, 1931, in *Revista de medicina y cirugia de la Habana*. Dr. Pérez Ara claims priority for the introduction of the catheter into the right heart through the internal jugular veins. He passed a Nelaton catheter up to the right auricle and, after injecting 20 c.c. of a 50 per cent solution of sodium iodide he made an exposure at the end of the injection. By this method he obtained very clear visualization of the lung vessels. Dr. Pérez Ara in this experiment, as did Egaz Monis in his *pneumoangiography*, used a normal thoracic x-ray technique. If they had used a more penetrating exposure, they would certainly have obtained the visualization of the heart chambers. This was the fundamental change in technique made by Castellanos and associates.[6-8]

In 1946 one of us, (A. Celis) who is mainly interested in lung and mediastinal problems, modified the method with good results and applied the modified technique to heart problems.

TECHNIQUE

The reasons why Castellanos' method does not give clear-cut results are the following: (1) the relatively long distance that the opaque substance must travel from the antecubital veins to the heart; (2) too much dilution of the opaque substance with nonopaque blood; and (3) a shunt of the opaque material to undesirable veins.

To avoid these defects it is necessary (1) to put the opaque substance in the place where it is needed, if possible; (2) to fill the part to be visualized completely; and (3) to inject the substance very rapidly to avoid too much dilution.

In addition to these conditions, the opaque substance must be very opaque to x-rays, nonirritating to the endothelium, nontoxic, and easily and rapidly eliminated.

The new method consists of the introduction of a rubber catheter directly into the right atrium, or right ventricle if desired, through the external jugular vein which has been exposed. Fluoroscopic control of the position of the catheter, determination of T.C.S. through the catheter, and a very rapid injection of radiopaque substance are necessary parts of the technique. We commonly use 50 c.c. of 70 per cent solution of diodrast, but we have used as much as 90 c.c. in very large hearts. The injection time should be 0.75 second to 1 second. We take films routinely during or at the end of the injection; others are made according to T.C.S. at intervals of one, two, and three or more seconds. The full technical details are contained in Celis' paper which is in press.

The dissection of the jugular vein and the introduction of the catheter through this vessel might seem dangerous. The procedures are really only impressive; they are not more dangerous than the introduction of a catheter through any other vein. The advantage of the jugular over the antecubital route is that the former permits the introduction of a sufficiently large catheter (number 12 or number 14) to make possible the rapid injection of enough material to produce correct opacification of the heart chambers.

It is interesting to note that in pyelography there have been fatalities. In spite of the fact that highly concentrated dyes are rapidly introduced while performing angiocardiography, no fatalities are known to have followed this procedure.*

NORMAL IMAGE

The excellent results obtained by these methods are similar to those obtained in post-mortem studies by Chapuon, Laubry, Cottenot, Routier, and Heim de Balsac in adults and by Castellanos in infants.

***After this paper was written, there was a fatal accident at the General Hospital. The patient had advanced rheumatic heart disease, with double mitral lesion and auricular fibrillation. Six hours after angiocardiography was performed, the patient had symptoms of pulmonary embolism and died three days later. Post-mortem examination could not be made, so we do not know what role the angiocardiography may have played.**

A careful review and comparison of their results with ours and with those obtained by American authors has enabled us to confirm some known facts and to discover others. The latter will be only briefly referred to in this paper since they will be the subject of more extensive research.

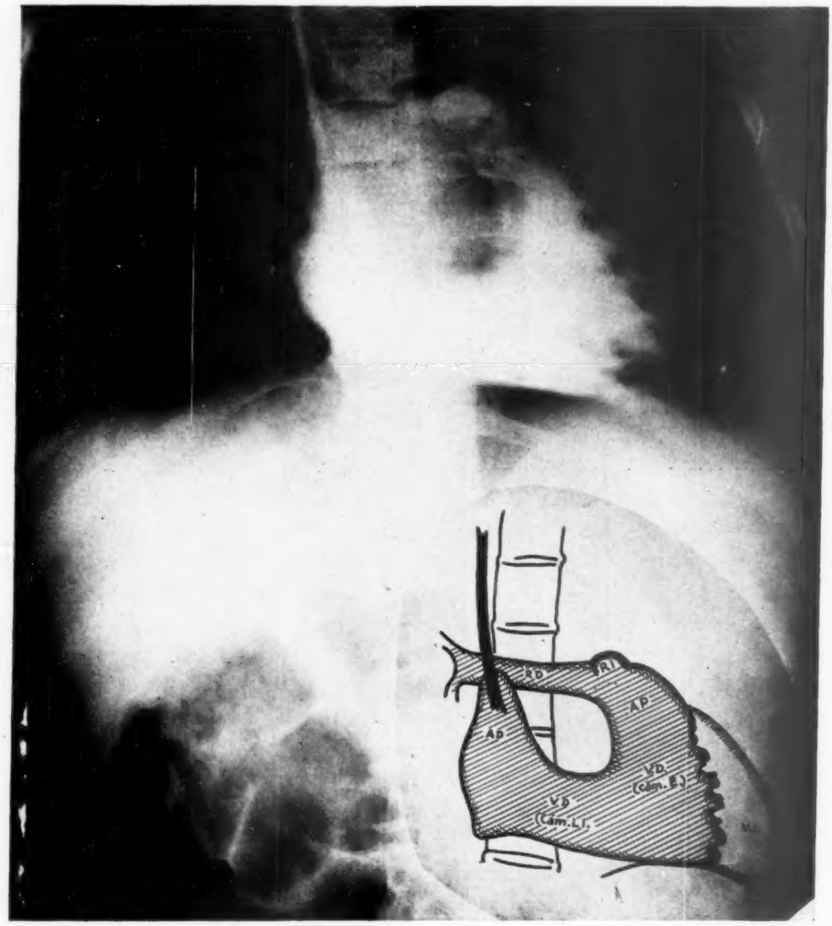


Fig. 1.—Angiocardiogram of right chambers of normal heart.

It is already well established that the right chambers are U shaped (Fig. 1). The superior vena cava and right atrium constitute the right limb of the U. Its projection is a little to the right of the vertebral column, and does not reach the diaphragm. The inflow tract of the right ventricle forms the horizontal limb. The outflow tract of the right ventricle forms the lower two-thirds of the left limb of the U; while the pulmonary artery forms the upper third of this limb. Between the right and horizontal limb, and between the lower two-thirds and

the upper third of the ascending limb there are often seen notches which we think are due to the tricuspid ring and to the pulmonary sigmoid valves respectively. We wish to point out (Fig. 2) that the pulmonary artery itself is not so near the

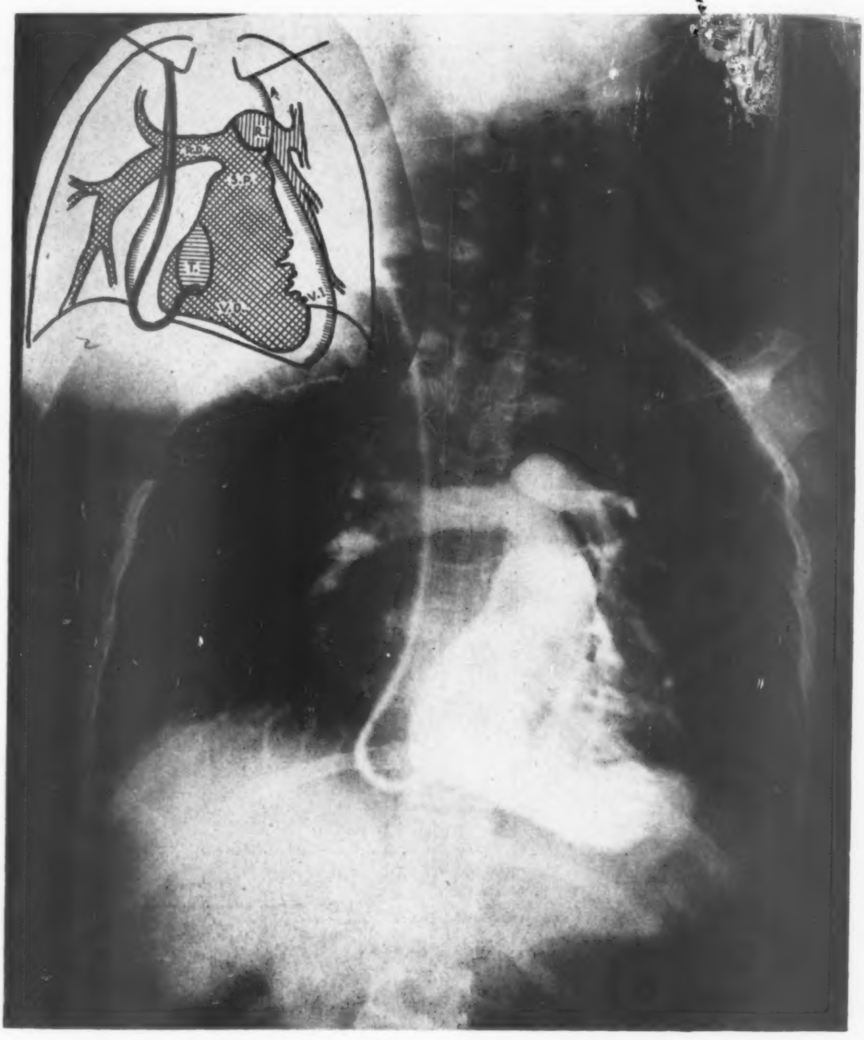


Fig. 2.—Angiocardiogram of normal heart. The pulmonary artery and branches are opaque. Relation of pulmonary artery to left border of cardiac silhouette is well shown (see text).

left border as has been thought. It is only the very highest part of the left middle arc of the cardiac silhouette that is formed by the pulmonary artery proper. The left branch comes off at a right angle to the main artery. The direction

of the left branch is at first backward but the course soon becomes a downward one. It is this descending branch and not the main pulmonary artery that forms the greater part of the middle arc of the left side of the cardiac silhouette. In other words, the left middle arc is formed in a very small part by the pulmonary

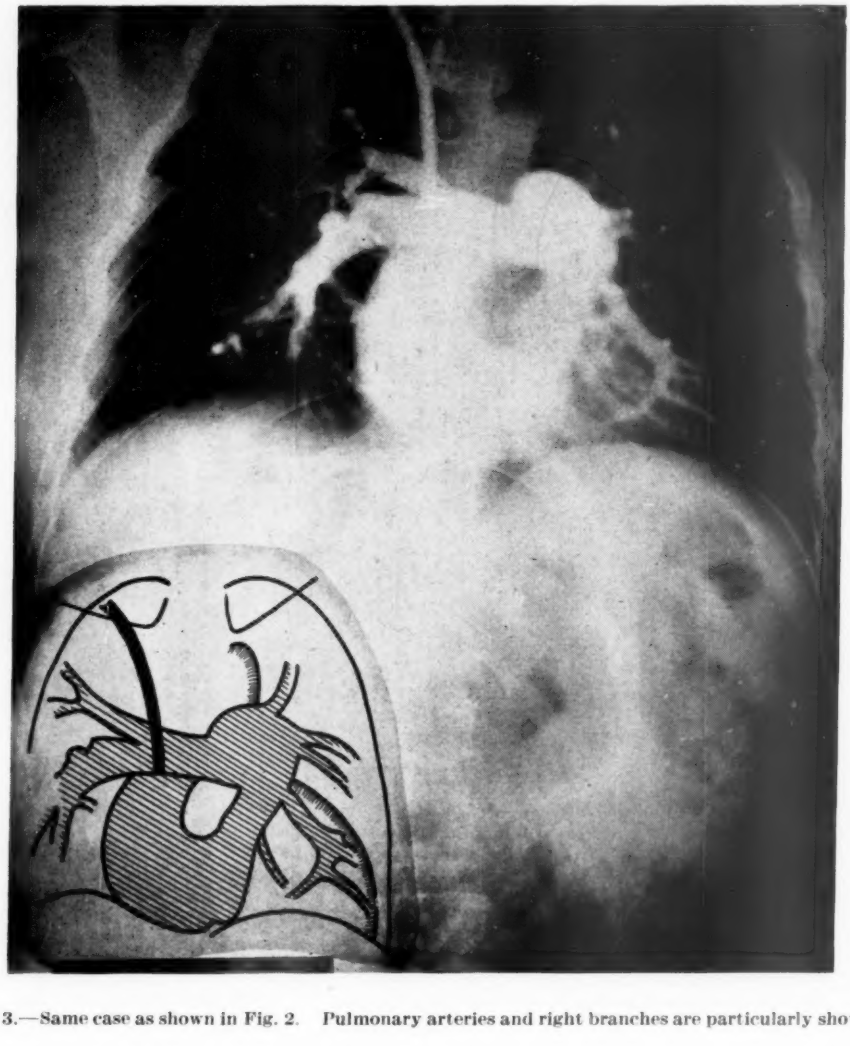


Fig. 3.—Same case as shown in Fig. 2. Pulmonary arteries and right branches are particularly shown.

artery itself; the rest is formed by the left descending branch. We have never seen the pulmonary conus placed so far to the left as to form a projection on the middle arc of the left border of the heart.

The right branch also comes off at a right angle, but its course is toward the right side of the chest. At approximately the right border of the vertebral column, it usually divides into two branches, less frequently into three. These branches spread outward rapidly. The right descendant branch is the largest. These branches are the most important shadows of the right hilum (Figs. 3, 4, and 5).

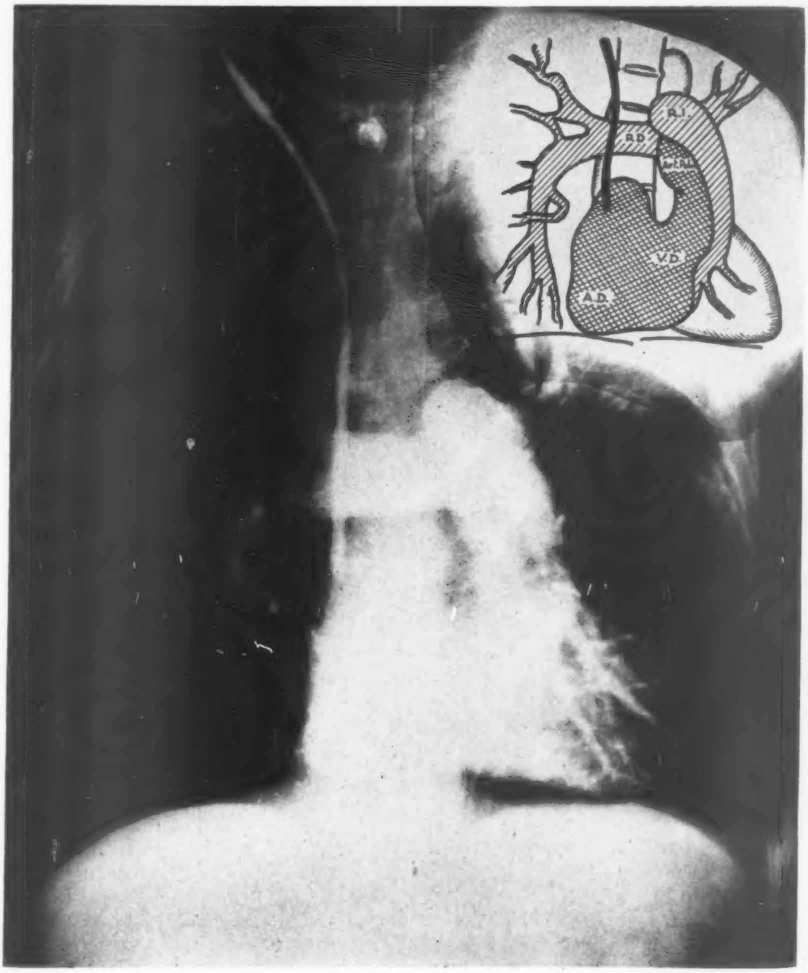


Fig. 4.—Same case as shown in Figs. 2 and 3. Pulmonary arteries and right branches are particularly shown.

We shall now describe the picture of the right heart in the lateral position (Fig. 6). In this position the superior vena cava is usually situated in the middle third of the chest. As it descends in a very gentle curve, it becomes

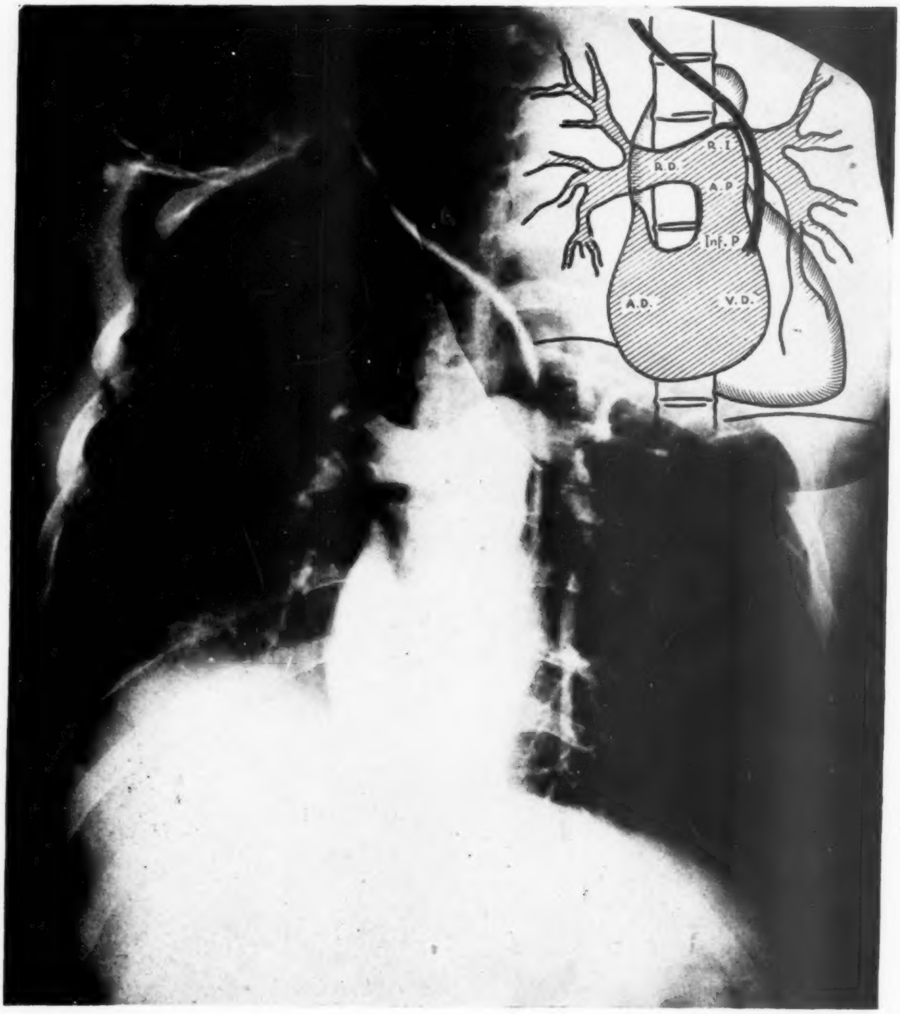


Fig. 5.—Same case as shown in Figs. 2, 3, and 4. Pulmonary arteries and right branches are particularly shown.

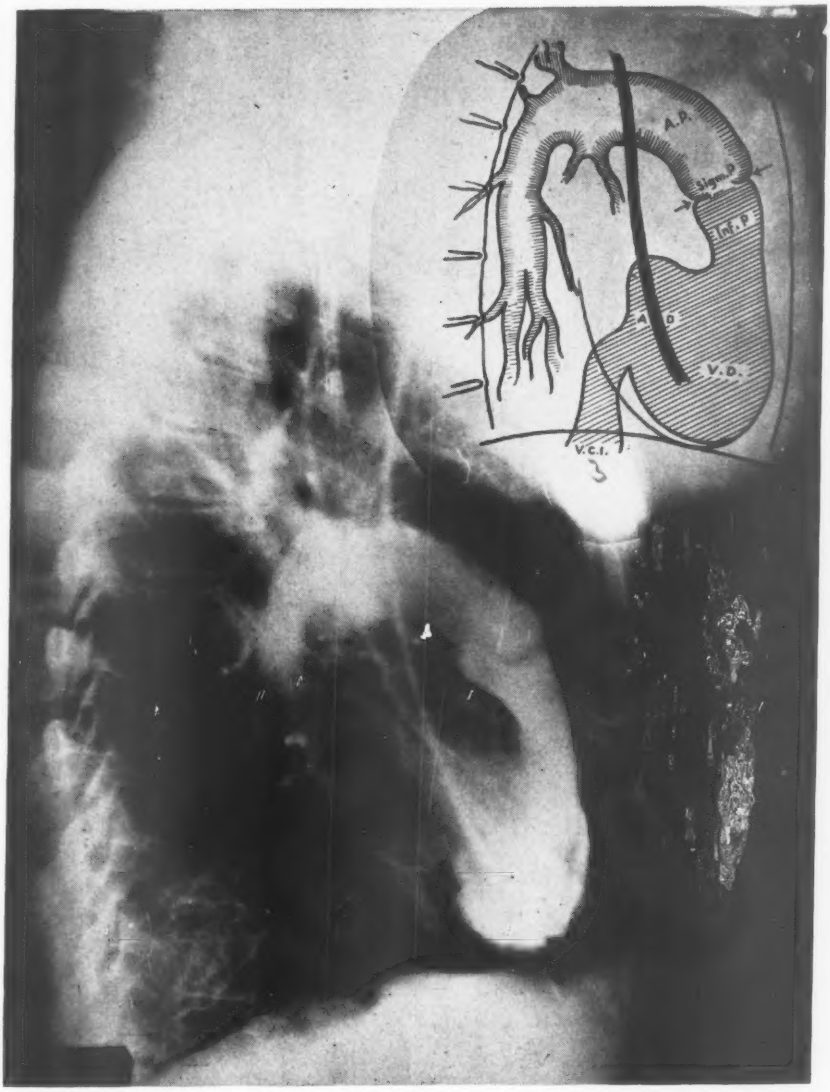


Fig. 6.—Angiocardiogram of right chambers of normal heart made in the lateral position.

widened and forms the shadow of the right atrium, which has a more or less oval shape in this projection. It is continued anteriorly by the inflow tract of the right ventricle which is visible in this projection. Ventrally there is the outflow tract of the right ventricle, which rapidly assumes an upward course

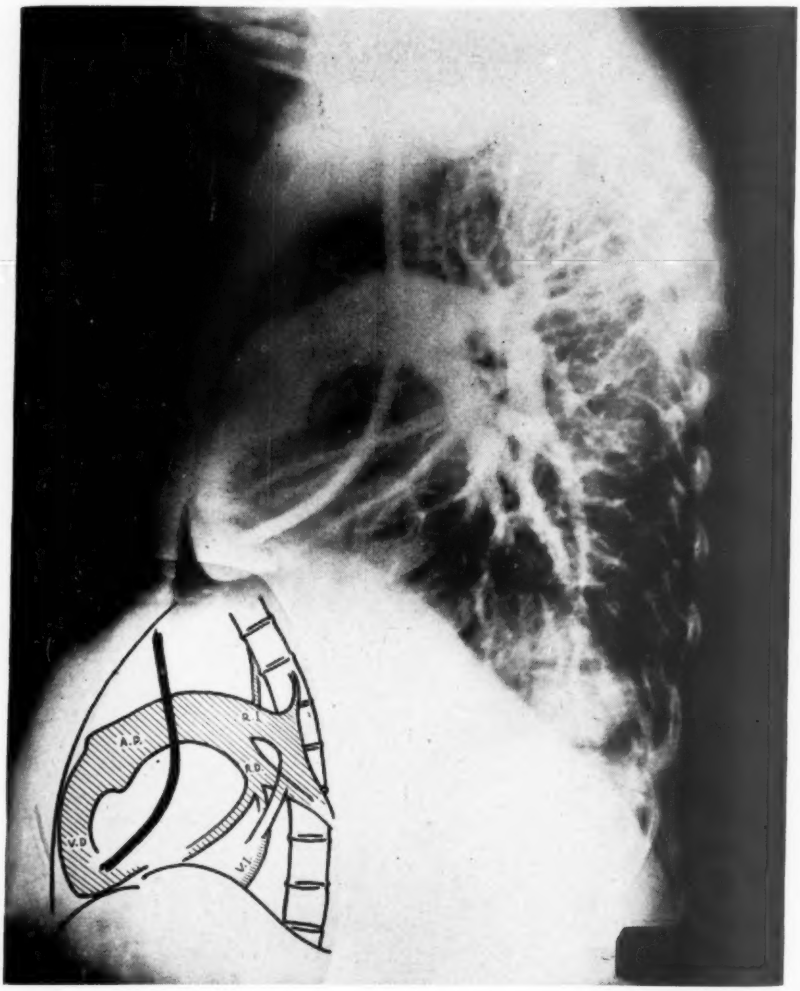


Fig. 7.—Angiocardiogram of normal right chambers and pulmonary artery. Lateral view.

until it joins the pulmonary artery itself. The diameter of the outflow tract of the right ventricle is about the same as that of the pulmonary artery. Between them, in the lateral position, are frequently seen the notches described in the frontal position, which we think are due to the pulmonary sigmoid valves (Fig. 7).

Beyond this notch the pulmonary artery takes a dorsal direction and divides into two branches, the right and left, which in turn divide into secondary branches. Quite often the opaque substance goes into the inferior vena cava (Fig. 8). The image of the injected right heart and the inferior vena cava resembles a sickle. When the opaque substance does not go as far as the inferior vena cava the image has a crescent shape. Castellanos calls this the "retort picture," since it recalls a well-known laboratory tool.

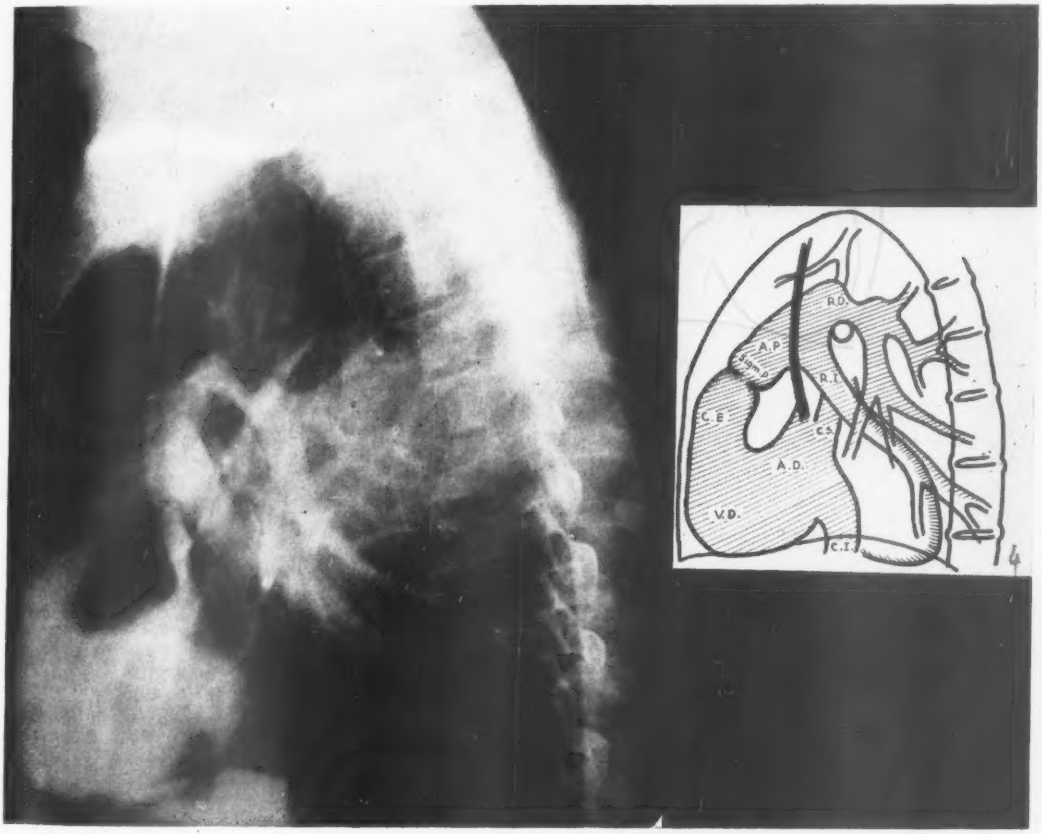


Fig. 8.—Angiocardiogram of normal right chambers and pulmonary artery. Lateral view. Note the filling of inferior vena cava.

IMAGE OF THE LEFT CAVITIES AND THE AORTA

If films are made a few seconds later, the pulmonary veins will be seen. These veins originate in the alveoli, and become more voluminous as they approach the left atrium. There are two pulmonary veins on the right side and two on the left. Two are situated cephalad, and two caudad. The left atrium soon becomes opaque (Fig. 9). Its shape resembles an "ace of spades," the apex

pointing caudad and to the left. Its shadow is superimposed on that of the vertebral column and corresponds more or less to the unfilled space of the right cavities, projecting between their limbs. Its left border is quite far from the heart's left border. The right side of the left atrium comes very near to the right

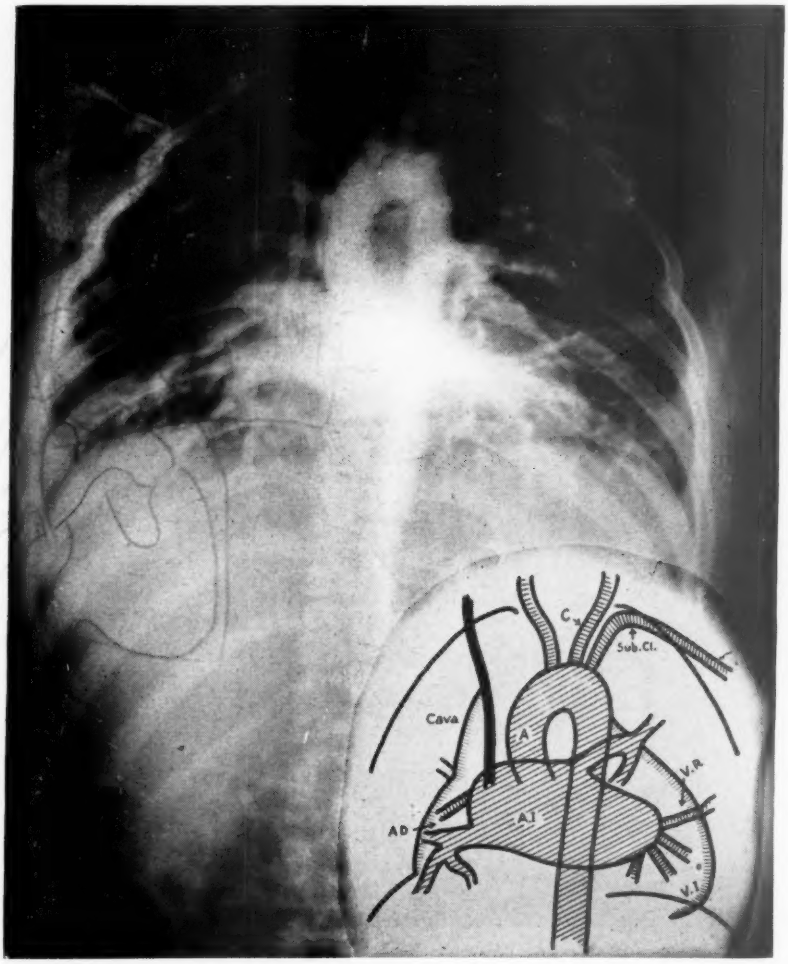


Fig. 9.—Angiocardiogram of normal left chambers. The left atrium is filled (see text).

border of the heart and very frequently the highest part of the right cardiac border is formed by the left atrium and not by the right. This fact makes it easy to understand why an enlarged left atrium frequently forms a double contour on the right side of the cardiac silhouette and why it infrequently forms a part of the left border of the cardiac silhouette. The filling of the left ventricle with the opaque substance also produces an oval shadow which is continuous

with the shadow of the left atrium, and extends as far as the apex of the heart. It is very common to see a deep notch between the left atrium and the ventricle. If we consider the picture of the atrium and the ventricle together they resemble roughly a figure eight.

Fig. 10.—Angiocardiogram made in systole (see text).

This picture is obtained when we catch the heart in diastole but it varies when the film is made during systole. In the latter case the aorta is completely filled; there is no filling of the left ventricle and usually, but not always, there remains some radiopaque substance in the left atrium. We have already pointed

out that the right ventricle is always visible, though its shape will vary in films taken during diastole and systole. The left ventricle usually empties completely during systole. A film made in systole will show the aorta to be completely filled but the left ventricle will not be visualized, unless there is some pathologic circumstance which causes part of the substance to be retained (Fig. 10).

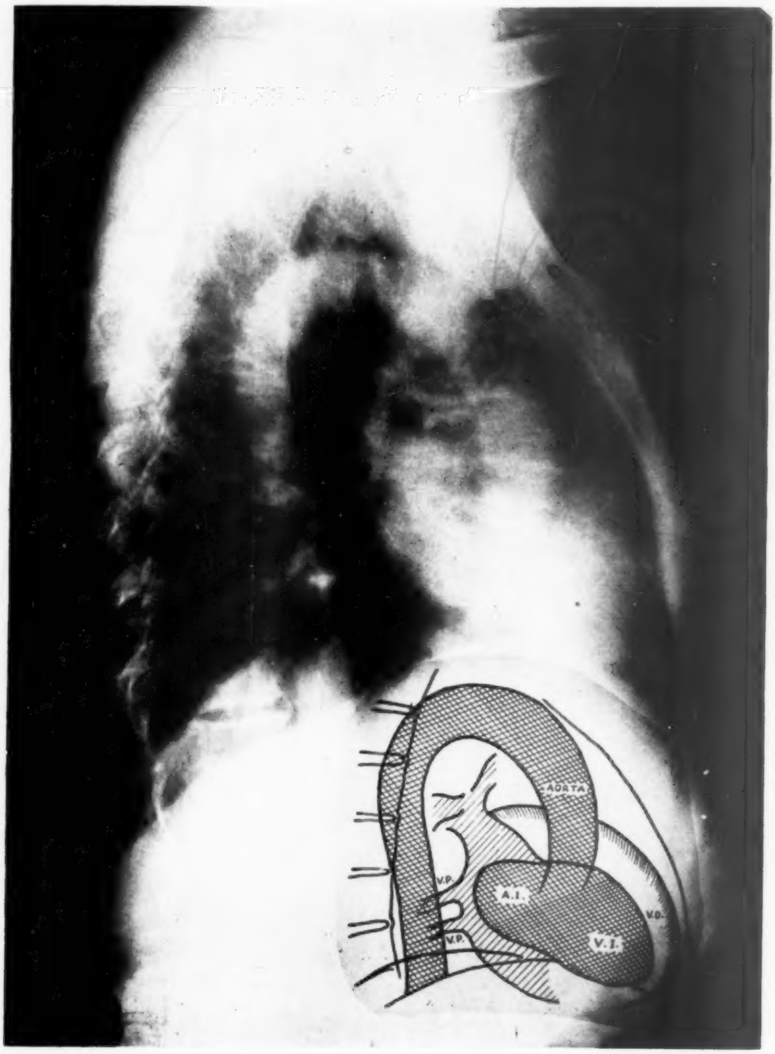


Fig. 11.—Angiocardiogram made in the lateral position. In this position the left chambers are not well visualized; the aorta and the pulmonary arteries are well visualized.

The complete filling of the left ventricle makes it possible to appreciate the location of the interventricular septum and in many cases the thickness of the ventricle wall. On the other hand, the inflow and the outflow tracts of the left

ventricle cannot be differentiated as they can be in the right ventricle; there is no demarcation between them.

Fig. 12.—Angiocardiogram of normal left chambers made in the lateral position. A notch marking the position of the aortic valves and a dilatation indicating the position of the sinuses of Valsalva are often seen (see text).

In the same anteroposterior projection the aorta is well visualized. It usually leaves the left ventricle at the level of the projection of the left border of the vertebral column. When the left ventricle is empty and the left atrium

still contains radiopaque substance, the aorta appears to come out from the left border of the atrium. Then it ascends more or less rapidly, depending on the shape of the heart, and then turns downward. The full descending aorta, the innominate artery, the two main carotids, and, lower down, sometimes the intercostal arteries can be visualized. Occasionally the completely filled renal arteries are seen.

The lateral projection (Fig. 11) is not very useful for visualizing the left chambers but it is useful for visualizing the pulmonary artery and the aorta; these structures are better seen in this position than in any other. The chambers of the left heart in this position are small. In the lateral projection the left chambers as a whole also resemble a figure eight. The aorta can be seen coming out from the left ventricle at about the upper loop of the figure eight; it rapidly ascends and is quite near the anterior chest wall. At this point an anterior and a posterior notch very similar to those seen in the pulmonary artery can be seen (Fig. 12). Immediately above the notch there is a slight dilatation. We think that the notch is due to the sigmoid valves and the dilatation to the sinuses of Valsalva. The situation of the aorta naturally varies according to the shape of the chest and to the age of the subject: in older people it is not so near the chest wall.

ABNORMAL IMAGES

In order to clarify description and to facilitate comparison with the normal images, we shall describe the pathologic images which will be described in the same order that has been used in describing normal hearts. The structures

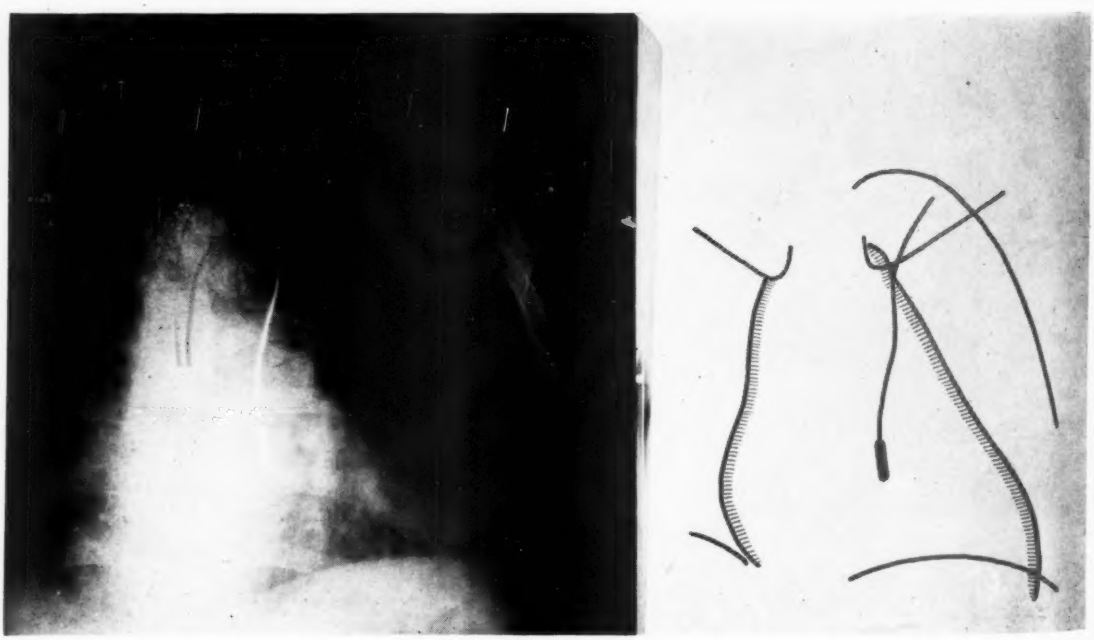


Fig. 13.—Angiocardiogram of a patient with persistent left superior vena cava.

and chambers will be discussed in the order on which they are visualized after the injection of the opaque substance. Two main contingencies may be present: (1) the substance may follow the normal circuit; or (2) it may follow an anomalous course, because of perforations of the septa, or the vessels do not have normal origins or connections, or there are abnormal communications between the vessels.

Fig. 14.—Ordinary x-ray film of patient with mitral and tricuspid stenosis.

Abnormal Images With Normal Routes of Flow.—The image of the *superior vena cava* is always perceptible. In most instances the injecting catheter is inserted into this vessel. Even when it is not possible to catheterize it, and when the injection has to be made into the jugular vein with a large-guage needle, the presence of the opaque substance makes possible the identification of the vena cava and the recognition of anomalies of this vessel. Fig. 13 shows a persistent left superior vena cava which is probably connected directly to the left

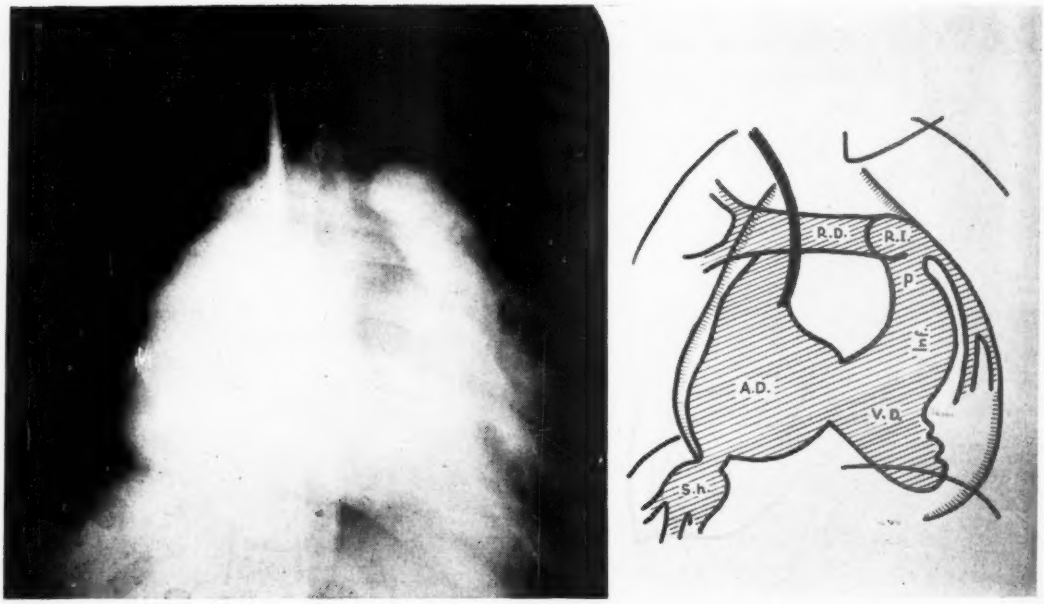


Fig. 15.—Angiocardiogram of same case shown in Fig. 14 (see text).

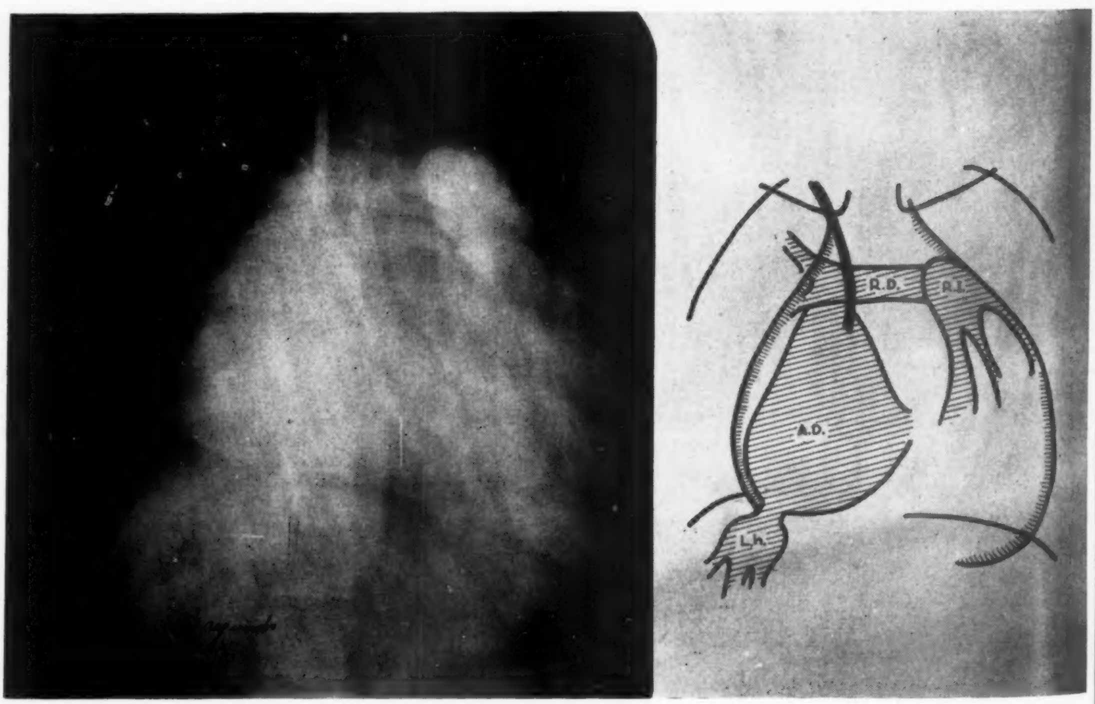


Fig. 16.—Angiocardiogram of same case shown in Figs. 14 and 15 (see text).

auricle. The electrocardiogram that was recorded indicated that the catheter which contained the electrode probably entered the right ventricle.

The *right auricle* is seldom seen as an isolated chamber. Since it empties promptly into the ventricle, the image obtained usually shows both cavities together. It is possible to see the auricle alone, however, when the ventricle empties and the auricle remains full; this is often the case in tricuspid stenosis, (Fig. 14). Here is an ordinary x-ray of a patient with rheumatic mitral disease and with a marked dilatation of the cavities. The angiocardiogram (Fig. 15)

Fig. 17.—Angiocardiogram of a patient with an aortic aneurysm which compressed the infundibulum of the pulmonary arteries. A notch caused by the tricuspid valve is seen.

at the end of the injection shows an enormous right auricle, clearly separated from the ventricle by a narrow zone corresponding to the tricuspid valve. In Fig. 15, however, the right ventricle is full, as well as the two branches of the pulmonary artery; but three seconds later, (Fig. 16), the ventricle has emptied while the auricle still retains the opaque substance: it remained full six and even ten seconds after the injection, when the aorta was already completely visible. The diagnosis of tricuspid stenosis in this case had escaped the clinical examination.

The image of the *right ventricle* may be missing or it may be greater than normal or, finally, it may show deformations. We shall discuss later the cases where it is not seen, since they depend upon complex malformations. Fig. 17 is a good example of an exaggerated enlargement of this cavity; it is prolonged

as far as the apex and reaches the left border of the heart, in contrast to a narrow and elongated expulsion chamber. The left branch of the pulmonary artery is clearly visible. This film was obtained from a patient with an aortic aneurism which compressed the region of the pulmonary infundibulum. In this same plate the notch marking the site of the tricuspid valve is seen. To the best of our knowledge this is the first time that this structure has been visualized.

Fig. 18.—An ordinary x-ray film of a patient with mitral stenosis.

We have also found this image of dilatation of the main *trunk of the pulmonary artery* and of its branches, and diminished size of the infundibulum in the course of rheumatic mitral stenosis, with no clinical sign to make us suppose that there was either a narrowing or a compression of the infundibulum. Fig. 18 corresponds to an ordinary mitral silhouette. The patient had a classical stenosing valvulitis. The protuberance whch deforms the medial arc makes us suspect that there is a greatly dilated left pulmonary branch. Actually, three seconds after the injection (Fig. 19), the trunk of the artery and its left branch are seen to be very

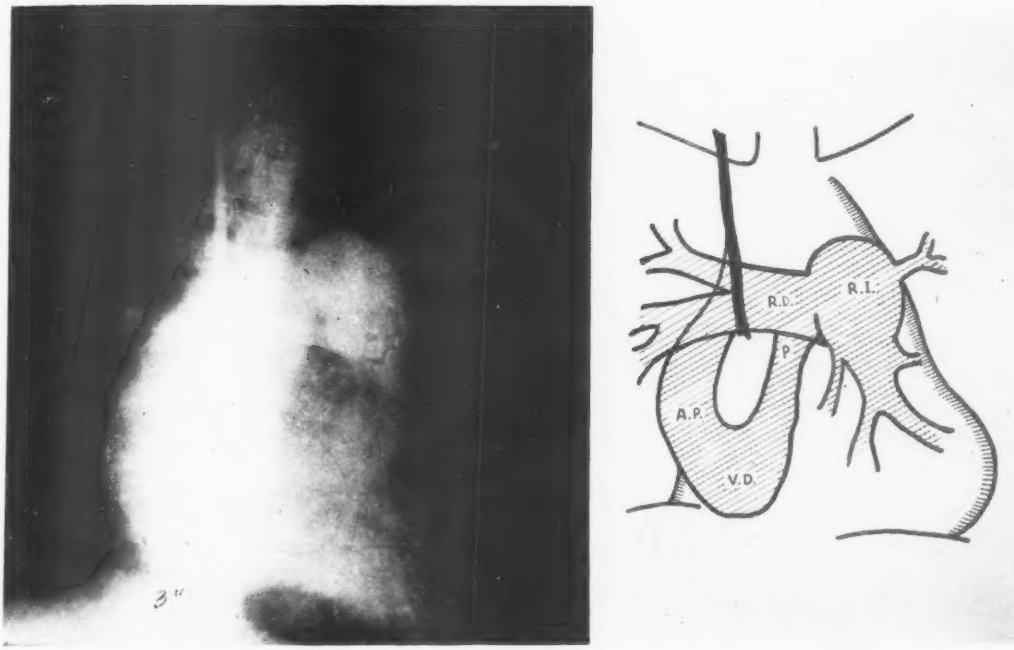


Fig. 19.—Angiocardiogram of same case shown in Fig. 18 (see text).

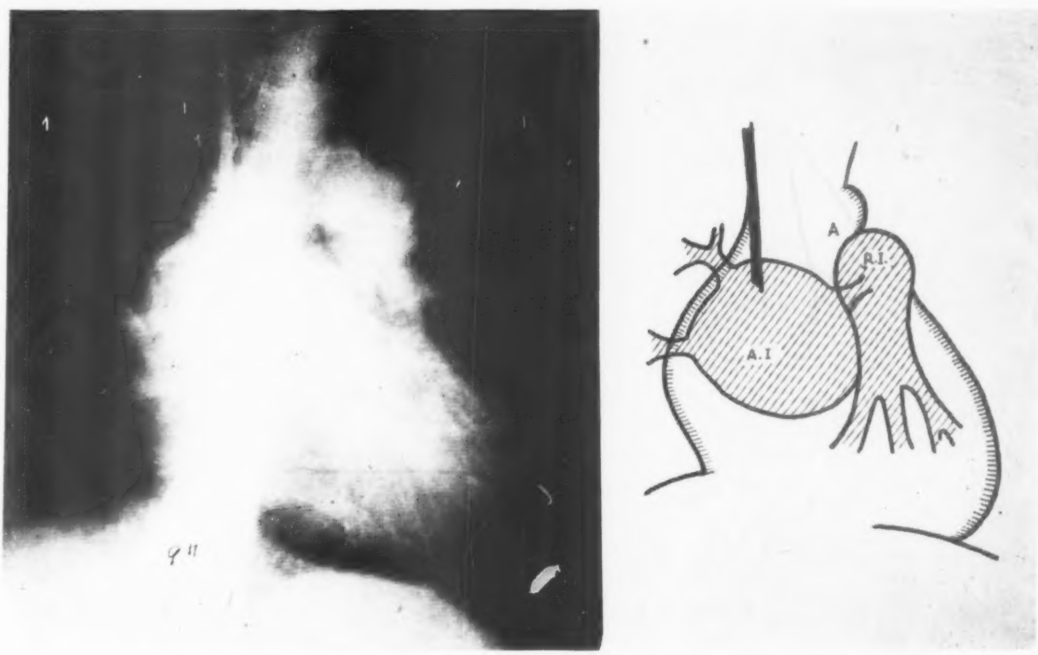


Fig. 20.—Angiocardiogram of same case shown in Figs. 18 and 19 (see text).

dilated. The infundibulum, on the other hand, can not be seen. Six seconds after the injection, the pulmonary and infundibular images are similar, and even three seconds later the arteries are still opaque (Fig. 20), although the left auricle is full. This plate provides a beautiful visualization of the isolated *left auricle,* only slightly enlarged but with a clear lower limit which corresponds to the mitral valve.

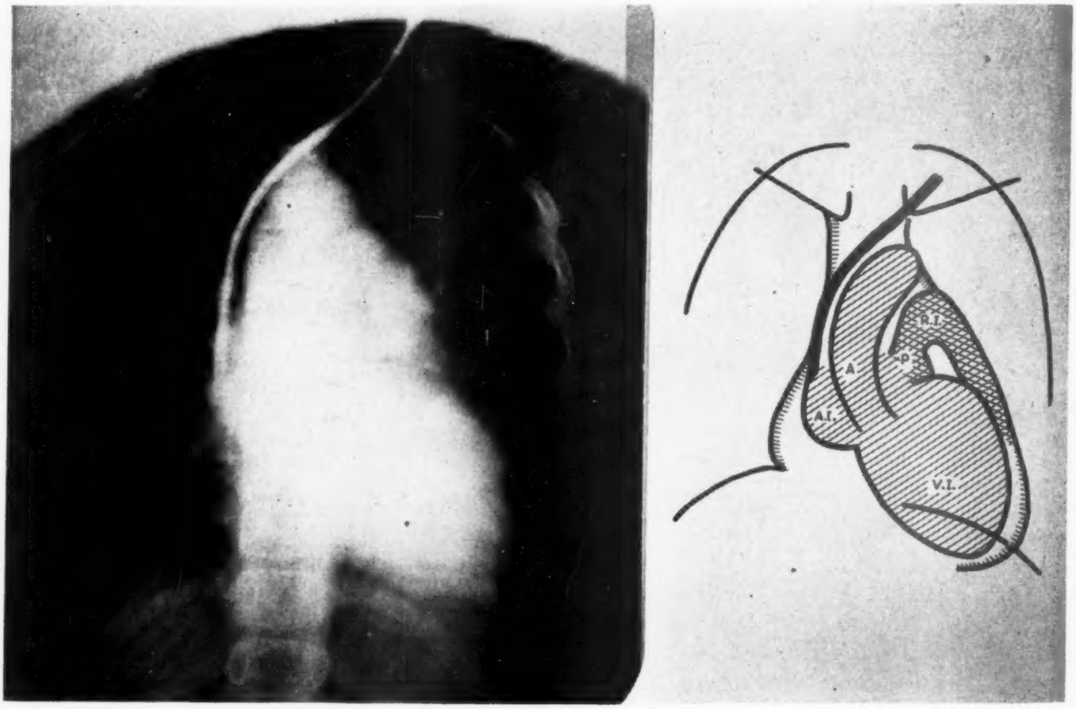


Fig. 21.—Angiocardiogram of patient with patent ductus arteriosus. The opacity of the pulmonary artery is maintained until the aorta is filled.

Regarding the left cavities, the most common occurrence is to find both chambers full at the same time. A marked enlargement of the *left ventricle* is clearly shown in Fig. 21. In this case an undiagnosed condition maintained the filling of the pulmonary artery up to the time of the filling of the aorta. This fact, as we shall see later, strongly suggests a persistence of the ductus arteriosus.

Angiocardiography yields very beautiful plates of the aorta and allows diagnosis to be made which may not be reached otherwise. A typical example is that of the case shown in Fig. 22, a simple x-ray film which shows an enormous prominence of the medial arc and a moderate cardiac enlargement of the right-sided type. The image strongly suggests an aneurysm, either of the pulmonary artery or of the aorta at the sinus of Valsalva. The clinical problem was not

easy. The patient, a 45-year-old man, had syphilis. The precordial region bulged slightly at its base, and there was a double beat. A slight systolic murmur and a somewhat louder diastolic murmur could be heard in the third left intercostal space. The radial pulse, however, was not of the collapsing type. Furthermore, the enlargement was of the right and not of the left cavities. The injection

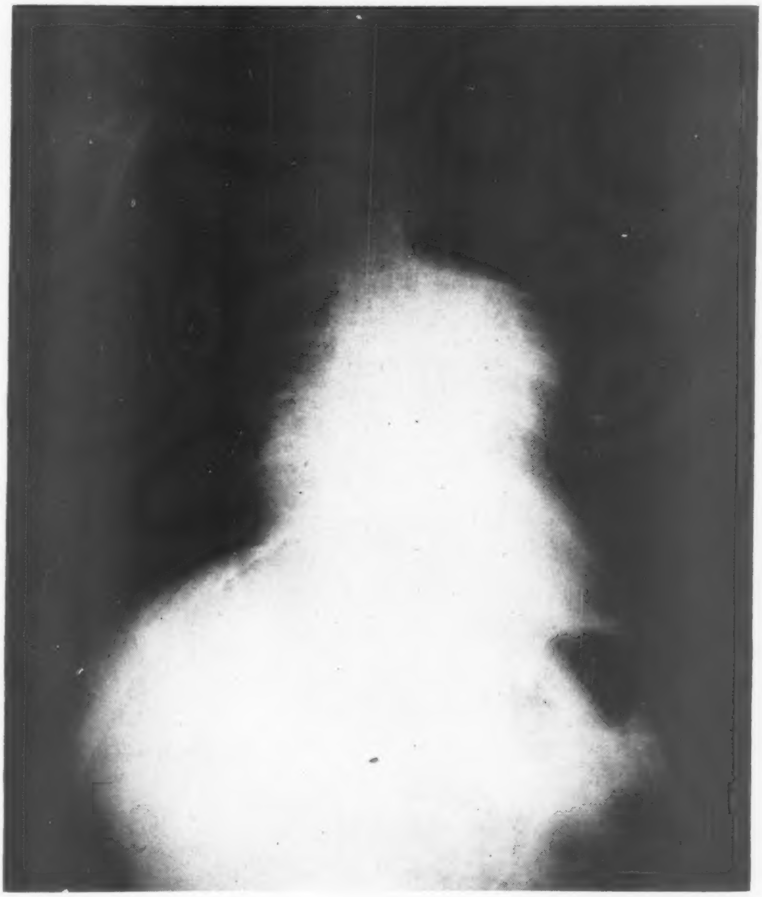


Fig. 22.—An ordinary x-ray film of a patient with an aneurysm of the left sinus of Valsalva which compressed the pulmonary infundibulum.

of opaque substance eliminated all doubts, (Fig. 23). At its end, the right cavities and the pulmonary artery with its branches were filled. The bulge, however, had not changed. The right cavities were clearly dilated and did not empty, either in four or in eight seconds, thus demonstrating the presence of an obstruction. When after twelve seconds they did empty (Fig. 24), the left ventricle and also the aneurysmal pocket and the descendent aorta were seen to

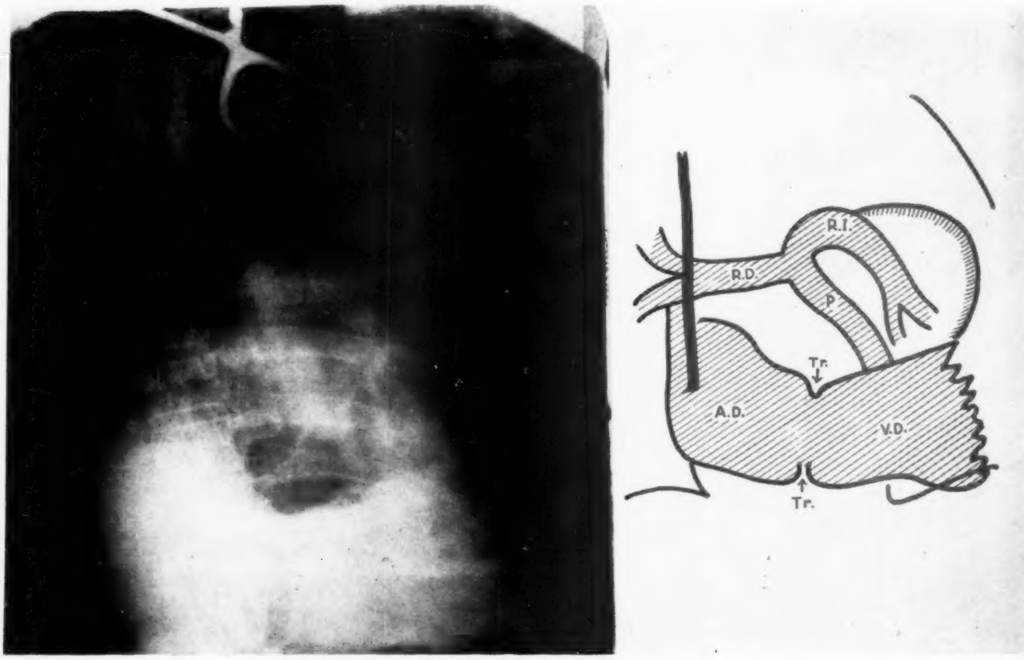


Fig. 23.—Angiocardiogram of same case shown in Fig. 22 (see text).

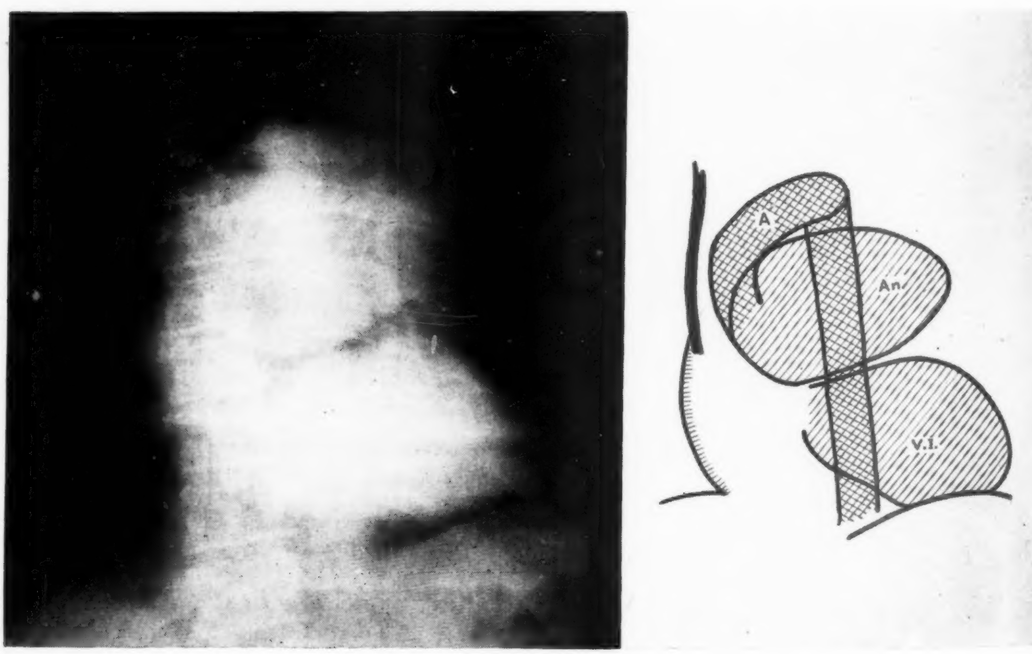


Fig. 24.—Angiocardiogram of same case shown in Figs. 22 and 23 (see text).

be filled. The diagnosis of *aortic aneurysm* of the left sinus of Valsalva with compression of the pulmonary infundibulum could be established with certainty.*

Not less interesting is the contribution of the method to cases of *isthmic stenosis* or *coarctation of the aorta*. In the ordinary x-ray film (Fig. 26), taken with a Bucky diaphragm and at a short distance in order to demonstrate Roesler's

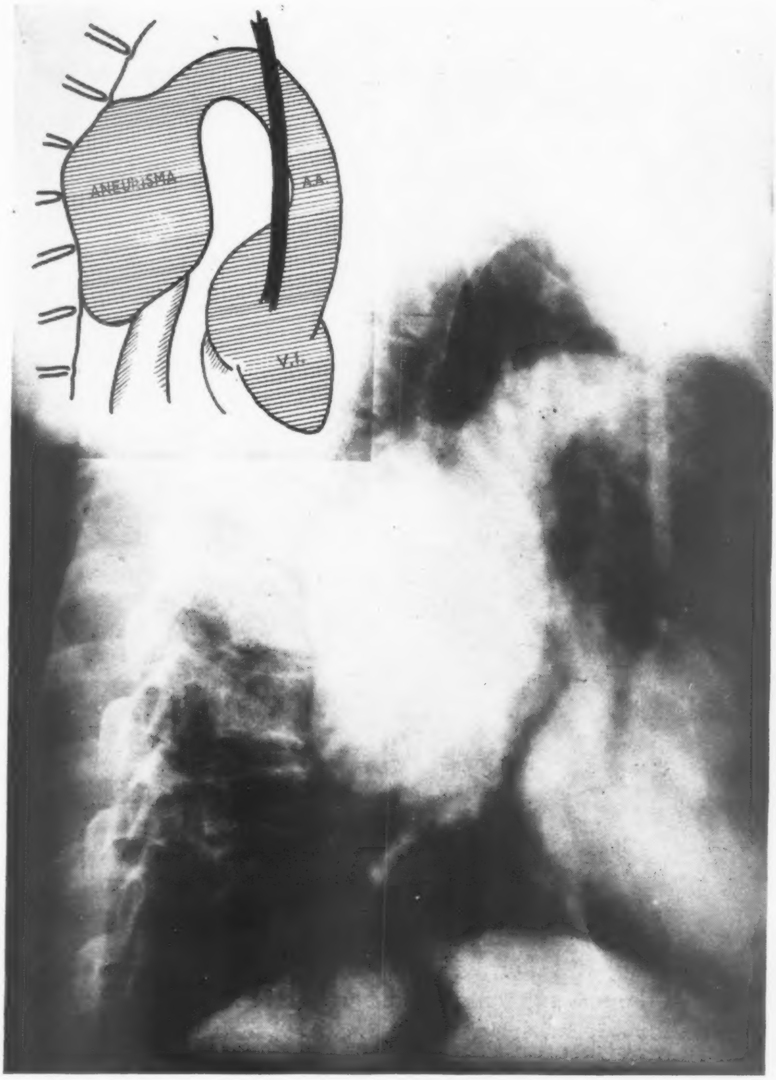


Fig. 25.—Angiocardiogram of a patient with a huge aneurysm of the thoracic aorta.

*In another type of aortic aneurysm the differential diagnosis from tumors can be established with precision. Fig. 25 shows a huge aneurysm of the thoracic aorta. It would be very difficult to demonstrate this by any other means.

sign of costal erosion, a quasi-normal cardio-aortic silhouette is seen with only slight enlargement of the left ventricle (confirmed later by a teleroentgenogram). In the lateral position at the end of an injection (Fig. 27) a splendid normal image of the right cavities and of the pulmonary branches is seen. Four seconds later (Fig. 28), on the other hand, the left cavities likewise appear normal, except for a thick ventricular wall. The ascending aorta and the transverse and initial portion of the descending aorta are all filled with the opaque sub-

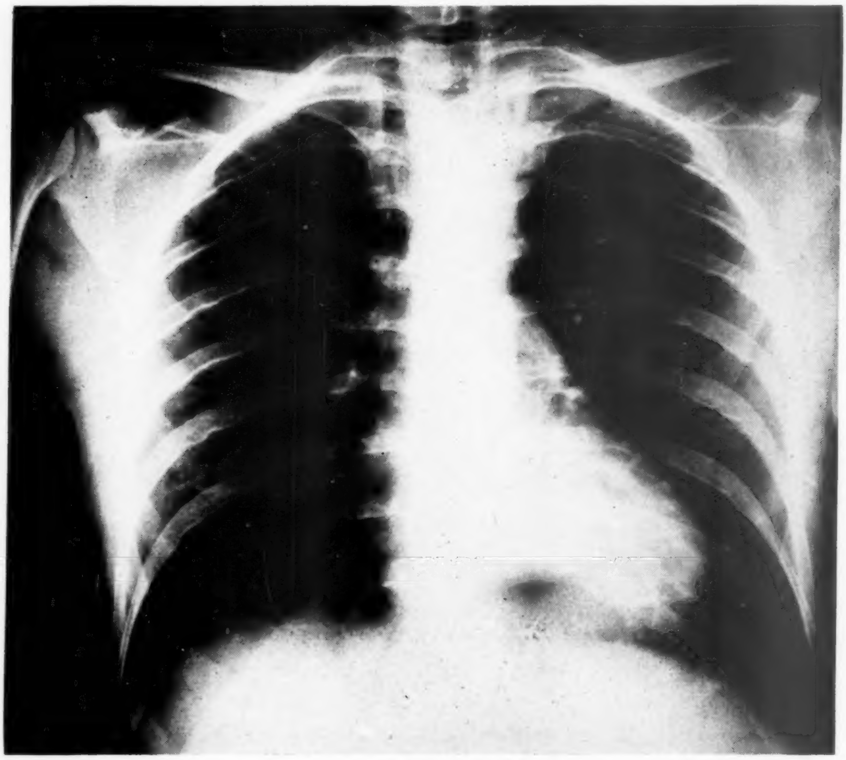


Fig. 26.—An ordinary x-ray film of a patient with a coarctation of the aorta.

stance up to the level of the intersection with the pulmonary artery. The six-second plate (Fig. 29) still shows a visible aortic arch and, also, a visible thoracic aorta. Between the two segments of the aorta there is a narrow zone, practically invisible and about 3 cm. long, where the two visualized segments approach each other by slender elongated tips. The narrowing is particularly noticeable in the image of the thoracic aorta, whose upper part is needlelike, and is followed immediately by a spindle-shaped dilatation about 6 cm. long, continued below by a narrow, hypoplasic aorta, which strongly contrasts with the wide ascending aorta.

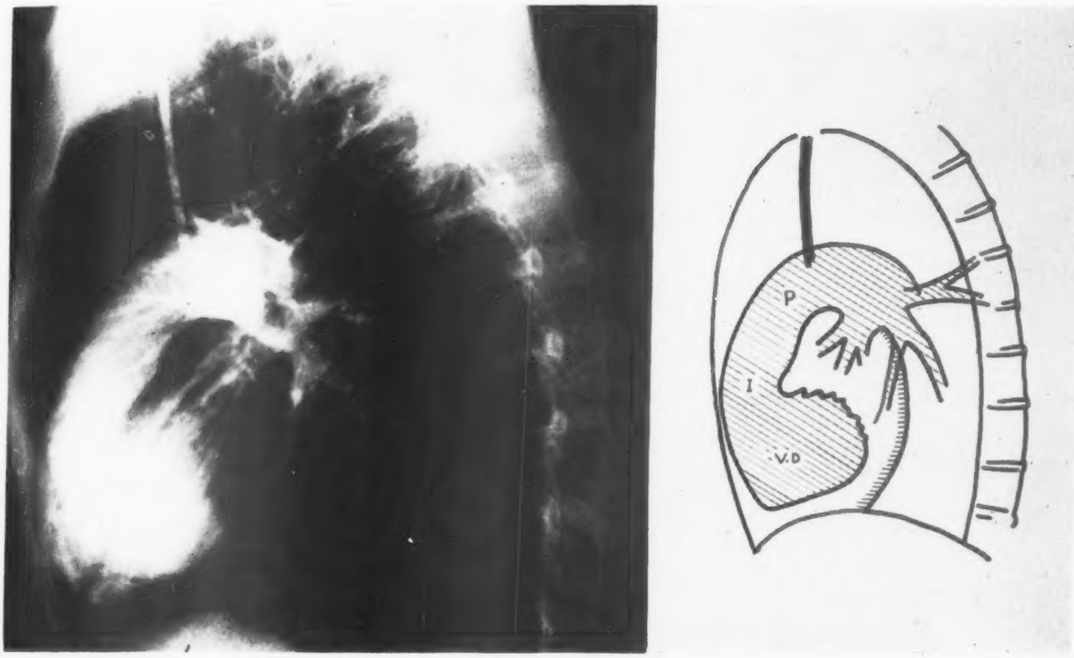


Fig. 27.—Angiocardiogram of same case shown in Fig. 26 (see text).

Fig. 28.—Angiocardiogram of same case shown in Figs. 26 and 27 (see text).

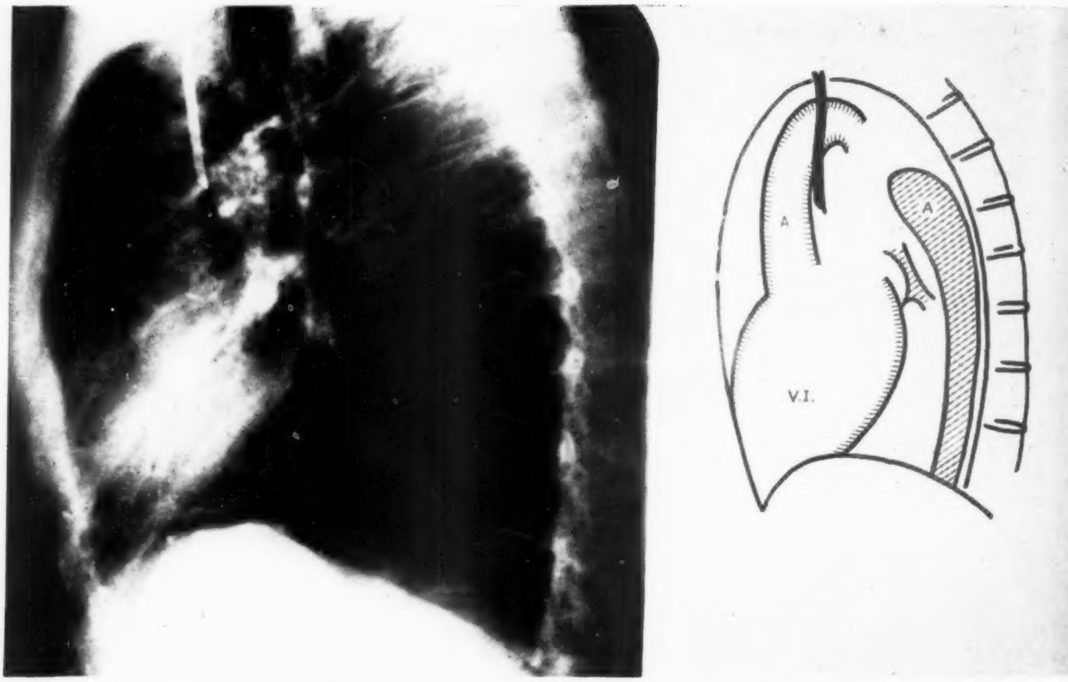


Fig. 29.—Angiocardiogram of same case shown in Figs. 26, 27, and 28 (see text).

Fig. 30.—An ordinary x-ray film of a 4-year-old child with cor biloculare or cor triloculare biatriatum with a persistence of a single arterial trunk.

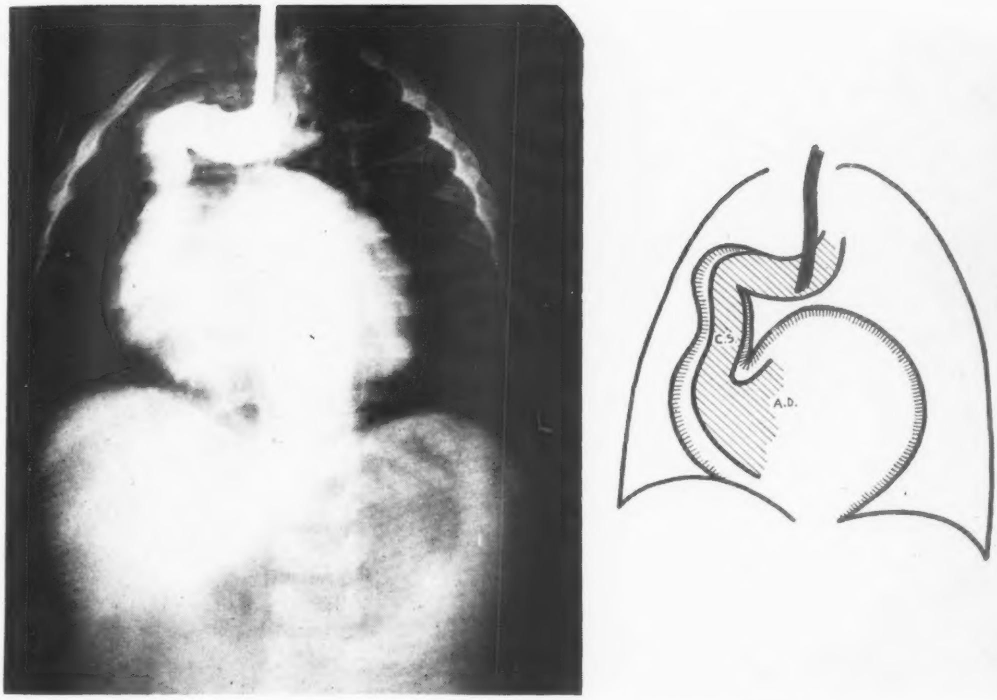


Fig. 31.—Angiocardiogram of same case shown in Fig. 30 (see text).

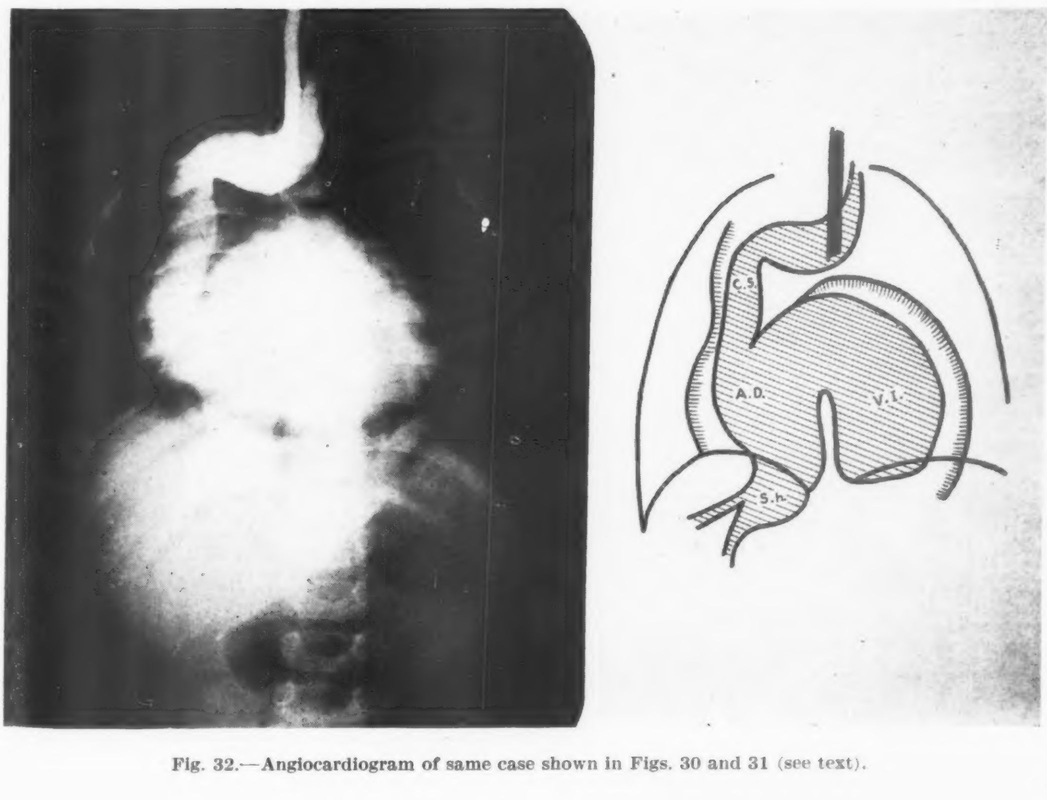


Fig. 32.—Angiocardiogram of same case shown in Figs. 30 and 31 (see text).

The films which we have described constitute, so far as we know, the first visualization of aortic coarctation that has been obtained in clinical medicine. This method gives valuable information concerning the site, degree, and extent of stenosis.

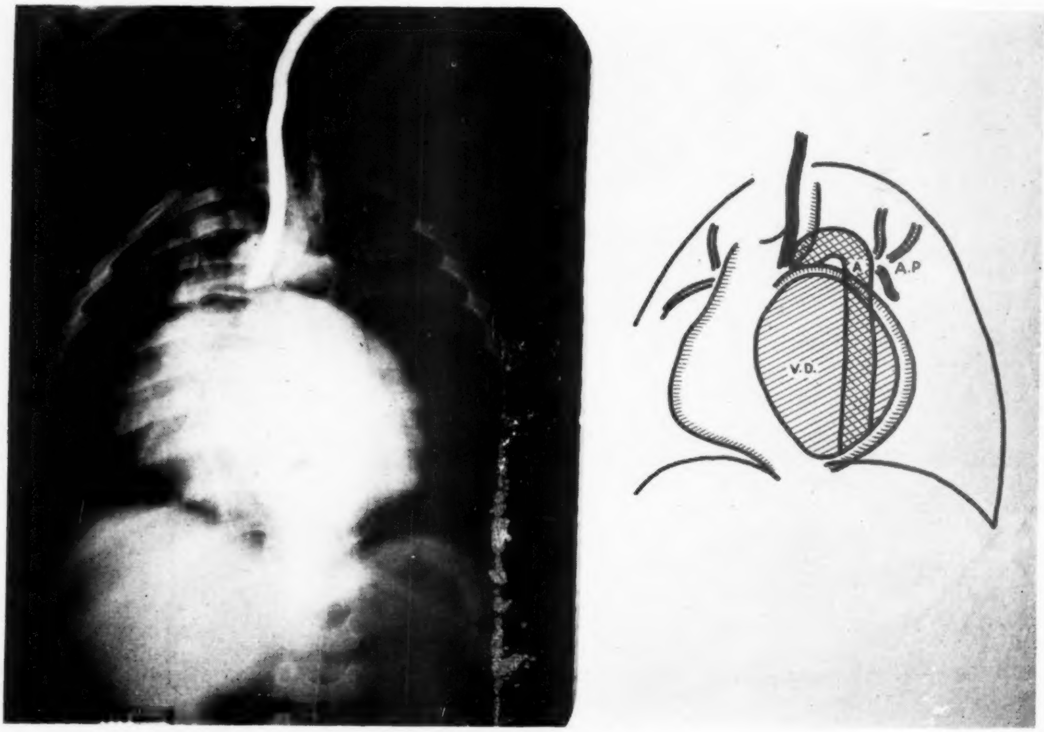


Fig. 33.—Angiocardiogram of same case shown in Figs. 30, 31, and 32 (see text).

Abnormal Images With Abnormal Routes of Flow.—It is in this field that the angiocardiographic method is of greatest value. It provides the only way of visualizing congenital abnormalities and atypical connections between the two circulations. The current of opaque substance may be followed through its abnormal route.

The patient whose film is shown in Fig. 30 is a 4-year-old child with congenital syphilis. He was intensely cyanotic and incapable of any effort. The heart was large. A systolic murmur, weak and somewhat musical, could be heard in the second left intercostal space and was transmitted to the vessels of the neck. The ordinary x-ray film shows marked enlargement of the left ventricle, a broad vascular pedicle, and an almost total lack of pulmonary trabeculae and vascular branches. Halfway through the injection (Fig. 31) the superior cava is visualized and appears large and displaced toward the right; its continuity with the right auricle is clear. One second later (Fig. 32), at the end of the injection, the right auricle is full as are the suprahepatic veins; but the left auricle and ventricle become filled at the same time. Still another second later (Fig. 33), the auricles

are already empty and only the enormous left ventricle, from which springs a narrow aorta, can be seen. At no instant was it possible to detect the right ventricle or the pulmonary artery. The few pulmonary vessels observed were seen to fill simultaneously with the aorta.

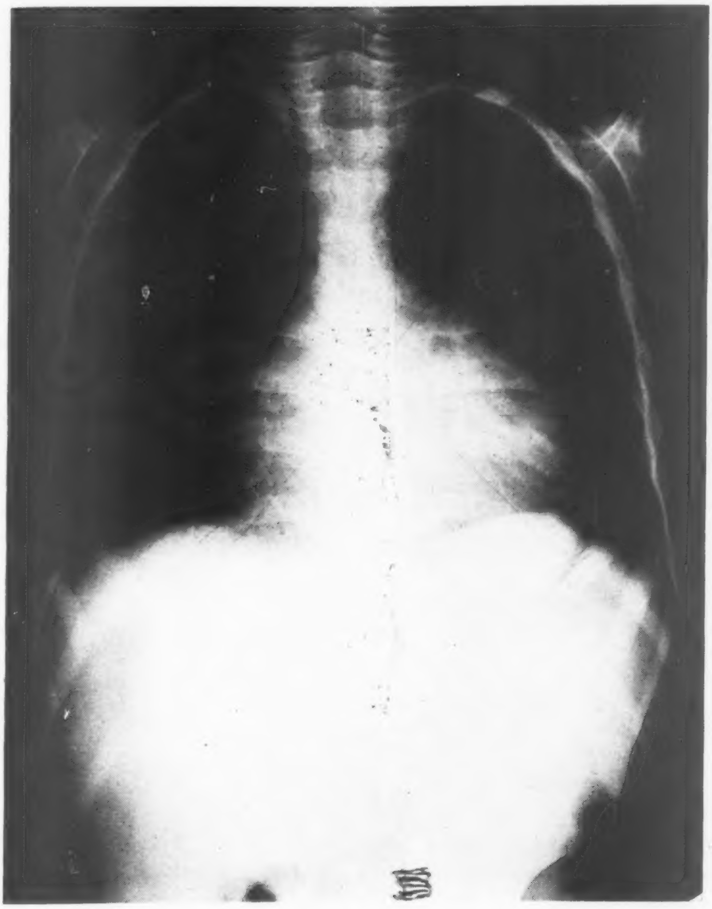


Fig. 34.—An ordinary x-ray film of a 4-year-old child with tricuspid atresia and cor triloculare with persistence of the truncus arteriosus.

The angiocardiographic data are eloquent: there is no right ventricle and no pulmonary artery, and both auricles are amply connected. The left ventricle is isolated and enormous. Clearly there exists a *cor biloculare,* or at most a *cor triloculare biatriatum,* with persistence of a single arterial trunk.

A somewhat similar case (Fig. 34) is that of another 4-year-old boy, very cyanotic since birth and with a soft systolic thrill and a harsh and loud systolic murmur at the second left intercostal space. The picture suggested a complex malformation with stenosis of the pulmonary artery, perhaps a tetralogy of

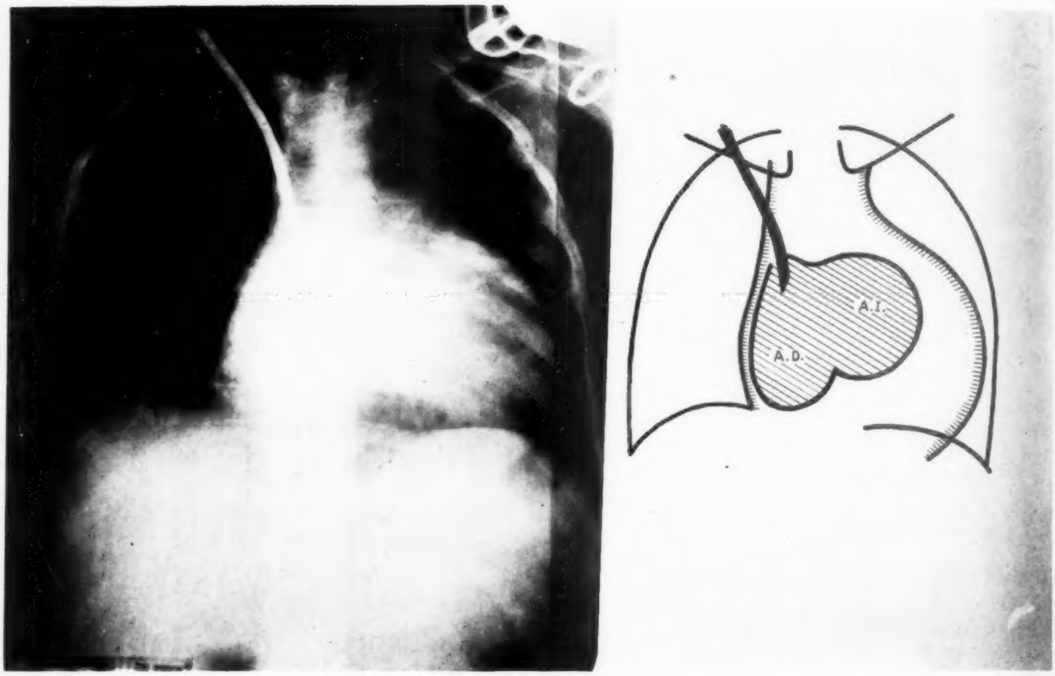


Fig. 35.—Angiocardiogram of same case shown in Fig. 34 (see text).

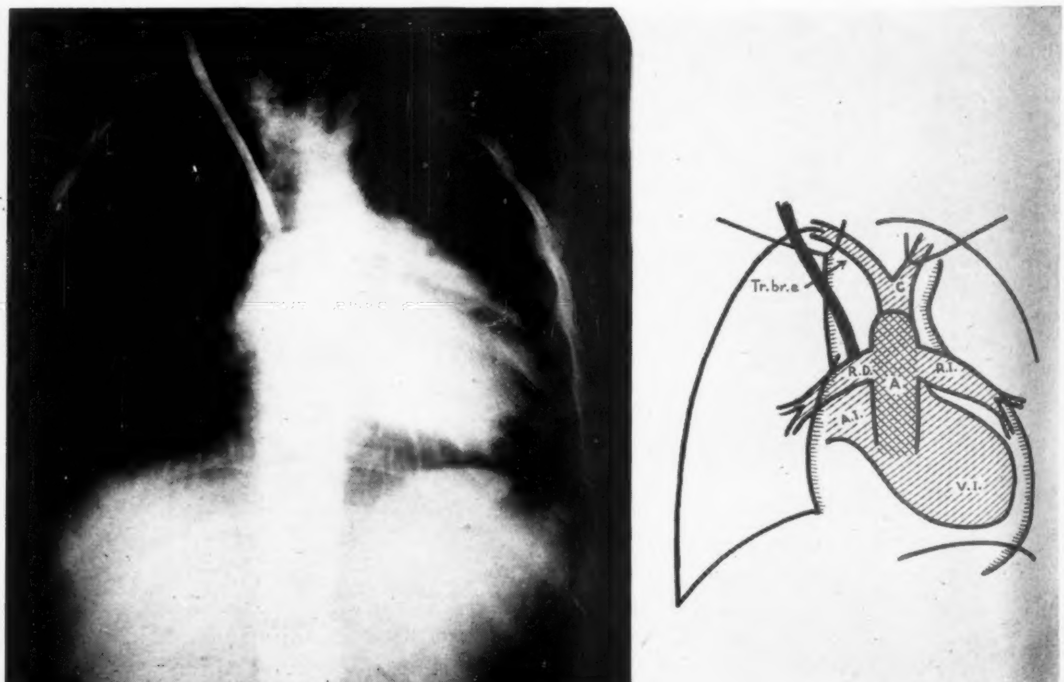


Fig. 36.—Angiocardiogram of same case shown in Figs. 34 and 35 (see text).

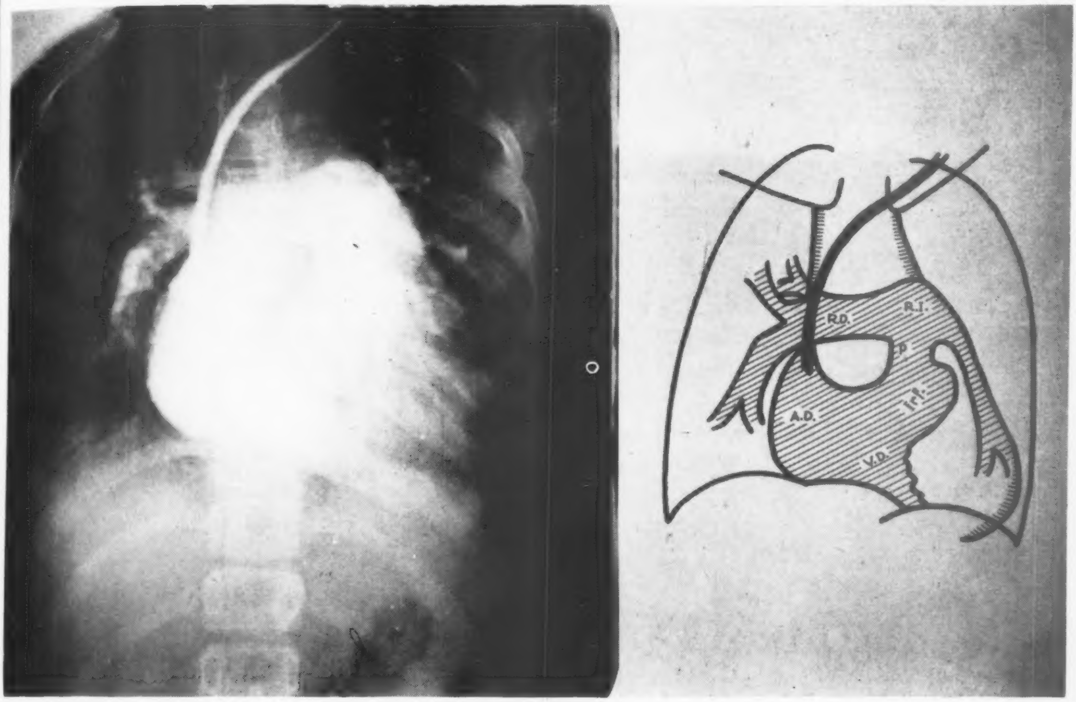


Fig. 37.—Angiocardiogram of patient with patent ductus arteriosus.

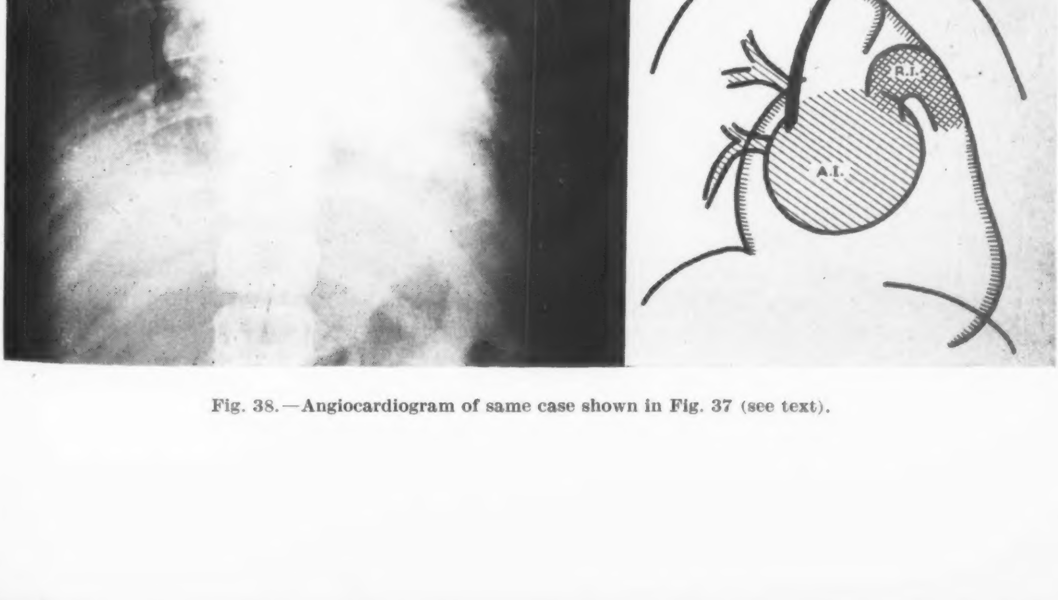


Fig. 38.—Angiocardiogram of same case shown in Fig. 37 (see text).

Fallot. Halfway through the injection (Fig. 35), both auricles are visualized and appear full and connected with each other, but separated by a clear notch. Subsequent plates, taken at one-second intervals, show a very hypertrophied left ventricle which fills first, and is then followed by filling of the aorta (Fig. 36). The left ventricle occupies a medial position and gives rise to two pulmonary branches. At no time was an image of the right ventricle obtained. These findings indicated a diagnosis of *tricuspid atresia* and *cor triloculare* with *persistence of the truncus arteriosus* instead of Fallot's tetralogy, which had appeared certain.

When Fallot's malformation or Roger's disease is actually present, the images are conclusive. Since we have studied mainly adults, we do not yet have any images of our own. The beautiful plates obtained by Castellanos[6-8] with his own methods may be consulted.

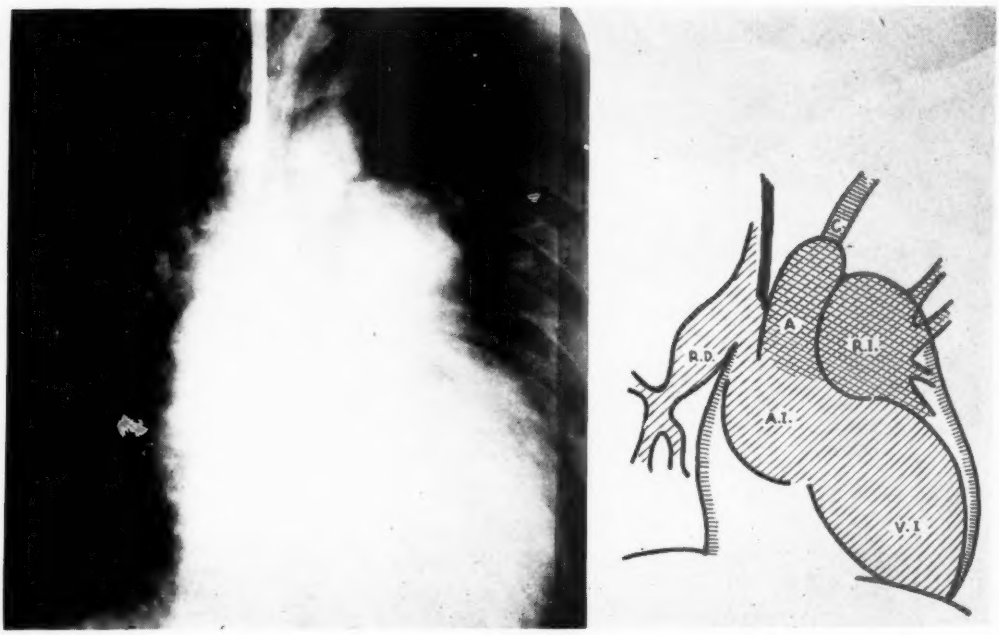


Fig. 39.—Angiocardiogram of same case shown in Figs. 37 and 38 (see text).

Finally, a new contribution of the method we are recommending and are presenting for the first time is its aid in diagnosing *patent ductus arteriosus.* It is not possible, of course, to visualize the duct itself, since it is usually so short that even the surgeon has difficulty in seeing it. The evidences of its existence are indirect. In Fig. 37, at the end of the injection, the right cavities are seen to be normal and full, with an accentuated prominence of the main trunk and the left branch of the pulmonary artery. Two seconds later, the pulmonary vessels are still full and the left auricle begins to appear. Two seconds later still (Fig. 38), the left auricle is clear and the left ventricle is beginning to fill. The opacity

of the pulmonary artery decreases from one plate to another. But in the next plate (Fig. 39), taken six seconds after the injection, in which the left ventricle as well as the aorta are totally opaque, the trunk and branches of the pulmonary artery, instead of completing the emptying initiated in the previous plates, again become opaque. This delayed back-flow filling of the pulmonary artery, at the time that the aorta fills, is a decisive radiologic sign: it is only possible if there is a fistulous connection between the two vessels. It is unnecessary to emphasize the importance of this sign in doubtful cases, especially now that this diagnosis carries with it the practical implication of surgical intervention.

REFERENCES

1. Forssmann, W.: Die Sondierung des rechten Herzens, Klin. Wchnschr. **8**:2085, 1929.
2. Forssmann, W.: Nachtrag zur der Arbeit, Klin. Wchnschr. **8**:2287, 1929.
3. Pérez Ara, A.: El Sondaje del Corazón Derecho, Rev de méd. y cir. de la Habana **36**:7, 1931.
4. Padilla, T., Cossio, P., and Berconsky, I.: Semana méd. **28**:5, 1932; **32**:11, 1932; **33**:29, 1932; **36**:41, 1932.
5. Egaz Moniz, Lopo de Carvalho, and Saldanha, A.: Angiopneumographie, J. de radiol. et d'électrol. **16**:469, 1932.
6. Castellanos, A., Pereiras, R., and García, A.: La Angiocardiografía, un método nuevo para diagnóstico de las cardiopatías congénitas, Archivos de la Sociedad de estudios clínicos de la Habana, 1937.
7. Castellanos, A., Pereiras, R., and García, A.: La Angiocardiografía en el niño, Séptimo Congreso de la Asociación Médica Pan Americana de la Habana, 1938.
8. Castellanos, A., Pereiras, R., and García, A.: L'Angiocardiographic Chez L'enfant, Presse méd. **80**:25, 1938.
9. Robb, G., and Steinberg, M. F.: Visualization of the Chambers of the Heart, the Pulmonary Circulation and Great Blood Vessels in Man; A Practical Method, Am. J. Roentgenol. **41**:1, 1939.
10. Thompson, S. A.: Differential Diagnosis by Means of Intravenous Contrast Medium of Two Cases Simulating Aneurysm of the Pulmonary Artery, Am. J. Roentgenol. **46**:646, 1941.
11. Steinberg, M. F., Grishmann, A., and Sussmann, M. L.: Angiocardiography in Congenital Heart Diseases, Am. J. Roentgenol. **48**:141, 1942.
12. Taylor, H. K., and Shulman, I.: Cardio-Angiography, Radiology **39**:323, 1942.
13. Steinberg, M. F., Grishmann, A., and Sussmann, M. L.: Angiocardiography in Congenital Heart Diseases. Patent Ductus Arteriosus, Am. J. Roentgenol. **50**:306, 1943.
14. Grishmann, A., Sussmann, M. L., and Steinberg, M. F.: Angiocardiographic Analysis of Cardiac Configuration in Rheumatic Mitral Disease, Am. J. Roentgenol. **51**:33, 1944.
15. Grishmann, A., Steinberg, M. F., and Sussmann, M. L.: A Typical Coarctation of the Aorta, With Absence of Left Radial Pulse, AM. HEART J. **27**:217, 1944.

THE SUBSTITUTION OF A TETRAHEDRON FOR THE EINTHOVEN TRIANGLE

FRANK N. WILSON AND FRANKLIN D. JOHNSTON, ANN ARBOR, MICH., AND CHARLES E. KOSSMANN, NEW YORK, N. Y.

THE early studies of the electrical phenomena associated with the human heartbeat carried out by Waller and by Einthoven and his associates led to the adoption of the leads from the two arms and the left leg which are still in universal use. For a great many years little thought was given to the possibility that these leads might be entirely inadequate in certain respects and that great progress in electrocardiographic diagnosis might be achieved by supplementing them with leads of other kinds. Some fifteen years ago, however, it became evident that leads in which one electrode is placed on the precordium and the other on some part of the body much farther from the heart are, to some extent, similar to unipolar leads from the ventricular surface, such as were used by Lewis and Rothschild,[1] and are capable of yielding information which limb leads cannot give. In the last decade, precordial leads have become indispensable.

This sequence of events raises the question as to whether further important advances in electrocardiography are likely to result from the development of still other new leads. If, like our predecessors, we may be overlooking opportunities in this direction, it is worth while to examine our present situation in the hope of ascertaining how we should proceed in order to take advantage of any such that may exist.

The general character of the heart's electrical field and the main features of the relations between it and the rise and decline of the excitatory process were clearly understood by Waller, by Einthoven, and by some of their contemporaries. These pioneers realized that, for certain purposes, the electromotive force of the heart may be regarded as a vector and that the limb leads are poorly suited to the study of the cardioelectric forces which are perpendicular to the plane defined by them. They knew also that these leads, unlike those from electrodes in contact with the heart's surface, yield a kind of average electrocardiogram which cannot be expected to depict variations in the excitatory process that involve only a small region of cardiac muscle and leave the general course of myocardial activation and recovery unchanged. At the start, it was, however, naturally difficult to interpret experiments in which direct leads from the ventricular surface were employed; the more so because of the inconstancy and variability of the form of the ventricular complex encountered in leads of this kind. These

From the Department of Internal Medicine, University of Michigan Medical School.
Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

variations were troublesome even though the factors responsible for them were understood. This probably explains why indirect leads came to be preferred to direct leads in experiments on animals in which the latter would have been much more useful.

The history of the development of our knowledge of electrocardiographic leads indicates that two courses are open to us in our attempts to find better methods of leading than we now possess. The first is to search for additional leads akin to unipolar precordial leads. These may be regarded as semidirect leads from the anterior ventricular surface. Such leads have a particularly favorable spatial relation to the cardiac muscle nearest the exploring electrode and they are capable of detecting lesions affecting it which are far outside the reach of any lead or combination of leads from electrodes that are distant from the heart. On the other hand, they are clearly unsuitable for discovering lesions so located that the exploring electrode cannot be placed much closer to them than to more normal parts of the myocardium. Since a semidirect lead from one cardiac region is necessarily an indirect lead from others, it is obvious that an adequate study of the whole heart by this method must involve the use of many leads. A relatively small exploring electrode must also be employed, for if a large one is used, the advantages gained by putting it close to the heart are lost through its short-circuiting effect.

Unfortunately, most of the epicardial surface is not accessible to exploration by semidirect leads. As far as the anterior ventricular surface is concerned, we can do fairly well by moving the exploring electrode step by step across the precordium, but the posterior ventricular surface is much farther from the skin so that unipolar leads from the back are far less effective than unipolar leads from the front of the chest. Unipolar esophageal leads are very useful for the purpose of studying certain auricular disturbances and often furnish important information in cases of posterior infarction. For the purpose of exploring all of the posterior ventricular wall they leave much to be desired. Worth-while information will certainly be gained by taking unipolar leads from the cavities of the right auricle and right ventricle which are accessible by catheterization. This procedure will surely prove a valuable one for research and may occasionally yield data of clinical value. On the whole, however, undeveloped possibilities of improving cardiac diagnosis through the exploration of additional parts of the epicardial surface by means of semidirect unipolar leads do not seem particularly promising.

The second course is to try to find the indirect leads that will give us the most useful over-all or average electrocardiograms with the full realization that such leads cannot be expected to supply information regarding abnormalities of the excitatory process that do not involve comparatively large regions of muscle. It is clear that the leads needed for this purpose will not be numerous so that the time required to take them will be small. The electrodes employed may be relatively large, and the use of such electrodes reduces to a minimum the difficulties due to the high resistance of the skin and to polarization. Neither the standard limb leads nor unipolar limb leads adequately meet our needs because they do not furnish sufficient information concerning variations in the excitatory

process affecting chiefly the sagittal components of the cardiac electromotive forces. By means of limb leads alone it is impossible to detect lesions confined to certain parts of the heart muscle and very difficult to differentiate peculiarities of the form of the electrocardiogram due to rotation of the heart about an axis that is nearly parallel to the frontal plane from those due to intrinsic cardiac disturbances.

Einthoven's early papers display his deep interest in the effects of rotation of the heart upon the electrocardiographic deflections and his method of finding the projection of the electrical axis of the heart upon the frontal plane was evidently an outgrowth of ideas that he had begun to develop years earlier. Many since his day have been equally conscious of this problem and have made important contributions bearing upon it. Nevertheless, much remains to be done. We have reached the stage where we know that rotation of the heart often has profound effects upon the form of the electrocardiogram which we have in the past attributed to other causes, but our ability to recognize these effects with certainty is still small.

The possibility of improving this situation by employing sagittal leads of one kind or another has occurred to many investigators. We regret that it is not possible to review the extensive literature on this subject. We shall refer only to the work of Arrighi,[2] of Buenos Aires. In his doctoral thesis, Arrighi analyzed a large series of tracings obtained by means of three leads which define a sagittal triangle. The apices of this triangle are a point on the left submaxillary region close to the chin, a point 3 or 4 cm. to the left of the midpoint of a line joining the umbilicus with the center of the pubis, and a point in the left interscapular region and approximately at the level of the spinous process of the seventh thoracic vertebra. Arrighi showed that his leads and the standard limb leads give the same value for the vertical component of the cardiac vector. He advanced cogent arguments in support of his contention that his leads permit an accurate estimate of the sagittal component of this vector. Our only criticism of his approach to the problem is that it involves the taking of three extra leads when only one should be required.

The fact remains that no method of determining the spatial electrical axis of the heart has been very extensively used either by him who originated it or by anyone else. One reason lies in the difficulty of measuring the error involved in any such method that is proposed and of demonstrating that by such means effects produced by rotation of the heart can be recognized with certainty. It seems probable that these difficulties will eventually be overcome.

DESCRIPTION OF AN EXPERIMENT ON A CADAVER

On March 1, 1934, we carried out an experiment on a cadavar for the purpose of ascertaining whether, by converting Einthoven's triangle into a tetrahedron, we could devise a reliable method of computing the position of the spatial electrical axis of the heart. The results of this single experiment, performed so long ago, are reported now chiefly for the purpose of laying the groundwork for future papers dealing with more recent work along the same line, and also because

they have a bearing upon the validity of Einthoven's triangle which has been the subject of a good deal of discussion.

The cadaver used was that of a man who had died more than a week before of carcinoma of the face complicated by pneumonia. During the interim the body had lain in the morgue in the supine posture, and it was suspected that, in addition to pronounced post-mortem changes, there had been considerable gravitation of fluid into the more dorsal tissues. The electrodes used to generate an electric field in the trunk consisted of two brass rods (25 cm. long) covered with rubber except at the sharpened tips. They were fixed in a wooden frame which kept them parallel and 5 cm. apart. This frame permitted the rods to be moved endwise, so that when they were thrust through the precordium, the depth of the tip of each was independently adjustable. After they were in place a potential difference of approximately 18 volts was rhythmically impressed upon these electrodes by means of a rotating contact breaker. Small copper disks with central binding posts sewn beneath the skin with the binding post projecting through it served as electrodes for the leads employed. One was placed on the lateral surface of each arm at the level of the insertion of the deltoid muscle and another on the inner aspect of the left knee joint. The fourth was placed on the back just to the left of the midline and at the level of the spinous process of the seventh thoracic vertebra.

The leads taken were standard Leads I, II, and III and leads from a central terminal to each of the four electrodes. These last leads will be referred to as Leads V_R, V_L, V_F, and V_B, respectively. On most occasions when these unipolar leads were taken, resistances of 10,000 ohms were used to connect the central terminal to the limb and back electrodes. Once 5,000 ohm resistances were employed. In a few instances the resistance between the central terminal and the back electrode was increased to 15,000 or 20,000 ohms or was removed. The effects of shifting the arm electrodes to the anteromedial margin of the shoulder joints and the leg electrode to a point just above the pubis were also investigated.

During the course of the experiment the electrodes used to generate the field occupied four different positions as follows:

Position A. Both electrodes in the third intercostal space. The minus electrode was close to the right and the plus electrode close to the left border of the sternum. The tip of the former was 5.7 cm. and that of the latter 8.8 cm. beneath the skin. The line joining these made, therefore, an angle of 32 degrees with the frontal plane. Its projection on this plane was parallel to the line of Lead I. The tips of the electrodes were 5.9 cm. apart, and their mean distance from the front of the chest was 7.25 centimeters.

Position B. Same as Position A except that the depth of the minus electrode was 5 cm. and that of the plus electrode 10 centimeters. The line joining their tips made an angle of 45 degrees with the frontal plane. This line was 7.1 cm. long and the depth of its midpoint was 7.5 centimeters.

Position C. The minus electrode was in the fourth intercostal space and the plus electrode in the third. Both were close to the left edge of the sternum. The tip of the first was 5.5 cm. and that of the second 10.7 cm. beneath the skin.

The line joining these tips was 7.2 cm. long and the depth of its midpoint was 8.1 centimeters. The angle made by it with the frontal plane was 46 degrees. Its projection on this plane was not quite perpendicular to the line of Lead I.

Position D. Same as Position C except that the tip of the minus electrode was 5.5 cm. and that of the plus electrode 15 cm. beneath the skin. The line joining the uninsulated tips made an angle of 62 degrees with the frontal plane. It was 10.7 cm. long and its midpoint was at a depth of 10.25 centimeters. The diameter of the chest from front to back was about 21 cm. so that the plus electrode was not more than 6 cm. from its posterior surface.

The measurements of the deflections in the various leads are given in Table I. Figures enclosed in parentheses were computed from those given in the other columns. Einthoven's E and his angle α were derived from the deflections in the standard limb leads in the usual way. At the time when the experiment was performed and before the results were known, the true angle α defined by the line joining the points where the input electrodes penetrated the anterior wall of the chest and the direction of Lead I was estimated at 0 degree for Positions A and B at -100 degrees for Positions C and D. It will be noted that the value of this angle computed by Einthoven's method differed from the estimate of the correct value by no more than 4 degrees for Positions A and B and by no more than 14 degrees for Position C. For Position D the difference was about 30 degrees. It was suspected that this large difference might be due to the gravitation of fluid into the more dorsal tissues, for it appeared when the plus electrode was thrust nearly three-fourths of the way through the chest.

The letter (*p*) following the capital letter which designates the position of the input electrodes in Table I indicates that the leg electrode was just above the pubis; the letters (*sp*), similarly used, indicate that, in addition, the two arm electrodes were on the anteromedial aspect of the shoulder joints. It will be noted that these changes in the positions of the electrodes had only trivial consequences. At the end of the experiment the distances from the three electrodes to the points where the brass rods penetrated the chest wall were measured. The distances of the right arm, left arm, and leg electrodes from the minus rod were 24, 18.5, and 37 cm., respectively. The distances of the same electrodes from the plus rod were 20.5, 16, and 41.5 cm., respectively. Since the electrodes were in the same position when Tracing 19 was taken as when Tracings 20 and 21 were made, these measurements throw no light upon the differences between Position C and Position D in respect to the magnitudes of the deflections in the limb leads.

Our chief purpose in making these observations was to ascertain whether Lead V_B would make it possible to measure the sagittal component of the electromotive force. Let us assume that the electrical field set up in the trunk by the voltage impressed on the input electrodes was equivalent to that produced by a centric doublet in a homogeneous spherical conductor. We may, then, consider the limb electrodes and the back electrodes the apices of a tetrahedron inscribed in a conducting sphere. If we regard this tetrahedron as equilateral, the distance between the plane defined by the limb leads and the doublet is equal to one-third of the radius of the hypothetical spherical surface. It may be shown

TABLE I

NUMBER OF TRACING	POSITION INPUT ELECTRODES	E	ANGLE ALPHA	I	II	III	V_R	V_L	V_F	V_B	RESISTANCE TO LIMB ELECTRODES	RESISTANCE TO BACK ELECTRODE
1	A	26.0	0	26.0	12.8	–13.0	—	—	—	—	—	—
2	A (p)	26.0	–3	25.8	12.0	–14.0	—	—	—	—	—	—
3	A	25.0	–1	25.0	12.0	–12.8	—	—	—	—	—	—
4	A	24.5	–2	(24.5)	(11.5)	(–13.0)	–11.5	13.0	0.0	—	10,000	—
5	A	24.0	–1	(24.0)	(11.5)	(–12.5)	–12.0	12.0	0.5	—	5,000	—
6	A	23.0	–1	(23.0)	(11.0)	(–12.0)	–11.0	12.0	0.0	—	10,000	—
7	A	23.5	–2	(23.5)	(11.0)	(–12.5)	–13.0	10.5	–2.0	3.5	10,000	10,000
8	A	23.0	–3	(23.0)	(10.5)	(–12.5)	–12.0	11.0	–1.5	2.5	10,000	15,000
9	A	23.5	–1	(23.5)	(11.5)	(–12.0)	–12.5	11.0	–1.0	2.0	10,000	20,000
10	B	24.1	–4	(24.0)	(10.5)	(–13.5)	–13.0	11.0	–2.5	4.5	10,000	10,000
11	B	23.8	–3	(23.8)	(10.8)	(–13.0)	–12.8	11.0	–2.0	3.5	10,000	15,000
12	B	23.0	–1	(23.0)	(10.0)	(–13.0)	–12.0	11.0	–2.0	2.5	10,000	20,000
13	B	23.5	–3	24.0	10.5	–13.0	—	—	—	—	10,000	10,000
14	C	36.3	–88	1.5	–30.5	–32.0	—	—	—	—	—	—
15	C	35.9	–87	(2.0)	(–30.0)	(–32.0)	9.5	11.5	–20.5	—	10,000	—
16	C	35.7	–87	(1.8)	(–30.0)	(–31.8)	8.0	9.8	–22.0	4.0	10,000	10,000
17	C	—	—	—	—	—	—	—	—	5.5	10,000	—
18	C (sp)	—	—	—	—	—	—	—	—	4.5	10,000	—
19	C (sp)	37.8	–86	(3.0)	(–31.0)	(–34.0)	8.0	11.0	–23.0	4.0	10,000	10,000
20	D (sp)	35.0	–70	(12.0)	(–22.5)	(–34.5)	–4.5	7.5	–27.0	24.0	10,000	10,000
21	D (sp)	35.5	–70	12.0	–23.0	–35.0	—	—	—	—	—	—

that if E is the manifest magnitude of the component of the doublet that is parallel to the frontal plane, and if β is the angle between this plane and the axis of the doublet, the deflection in Lead V_B should be $\frac{1}{4}\sqrt{6}\,E$ multiplied by tangent β. We are here supposing that the resistances connecting the central terminal to the four electrodes are equal.

On the other hand, we may suppose that the plane of the limb leads passes through the center of the spherical surface and, therefore, through the doublet. It may be shown that, in this case, the deflection in Lead V_B should be $\frac{E}{\sqrt{3}}$ multiplied by tangent β, when the central terminal is connected to the limb electrodes only. Before we compare these theoretical values for the deflection in Lead V_B with the values obtained experimentally, it is necessary to point out that the effect of removing the resistance between the terminal and the back electrode, or of making this resistance a multiple of the three equal resistances joining the terminal to the limb electrodes, may be easily computed. If we start with four equal resistances and disconnect the back electrode from the central terminal, without disturbing the other connections, the deflection in Lead V_B should increase by one-third of its original value. If we double the resistance between the back electrode and the terminal instead of removing it, the deflection in Lead V_B should increase one-seventh of its original value; if we increase this resistance by 50 per cent, the size of the deflection in Lead V_B should increase one-eleventh of its original value. The experimental data are not in accord with these predictions, but they are too few and the changes in the size of the deflection concerned are too small to be regarded as decisive. The predictions involve simple algebraic calculations and Kirchkoff's second law, and can, therefore, hardly be at fault.

It will be seen at once that the deflections recorded in Lead V_B are all much smaller than anticipated. Since the two hypotheses with regard to the position of the plane of the three leads with respect to the centric doublet lead to only minor differences in the theoretical size of the deflections in this lead, it will suffice if the values given in Table I, modified in each instance to the extent necessary to eliminate the effect of the resistance inserted between the central terminal and the back electrode, are compared with the value of $\frac{E}{\sqrt{3}}$ tangent β. The latter is 8.3 for Position A, 13.9 for Position B, 21.1 for Position C, and 38 for Position D. Increasing the magnitude of the sagittal component by altering the relative depth of the two input electrodes always changed the size of the deflection in Lead V_B in the proper direction, but the amount of the change did not bear a constant relation to that predicted. Position B should have yielded a deflection 50 per cent larger than that given by Position A. The actual increase in the size of the deflection was less than 30 per cent. Position D should have given a deflection about twice as large as Position C; it gave a deflection about six times as large.

We attribute the unexpectedly small values for the deflections in Lead V_B obtained in this experiment to the gravitation of fluid into the more dorsal tissues. Whether this opinion is or is not well founded, only additional experiments of a

similar kind can decide. It is not worth while at present to speculate regarding other possibilities. We may also call attention to another result that was unexpected. The rods used as input electrodes were parallel and always 5 cm. apart, and they were always perpendicular to the anterior chest wall. The input voltage was not varied. It is surprising, therefore, that the value of E should be 25 mm. for Positions A and B and about 35 mm. for Positions C and D. Unfortunately, neither the resistance between the input electrodes nor the magnitude of the current flowing between them was measured. A lower resistance, and consequently a larger current, would be expected to increase the value of E, even though the voltage applied remained constant. In the absence of such measurements, we cannot explain satisfactorily why E had one value when the frontal component of the input voltage was parallel to Lead I and another when it was roughly perpendicular to this lead.

SUMMARY

In an experiment on a cadaver, a potential difference was rhythmically impressed upon two small electrodes thrust into the heart or its immediate neighborhood.

The resulting differences in potential between a central terminal and four electrodes connected to it through equal resistances were recorded with the string galvanometer. The four electrodes were on the two arms, the left leg, and the left interscapular region.

By assuming that the electrical field generated in the trunk was equivalent to that of a centric doublet in a homogeneous spherical conductor and that the four electrodes were at the apices of a tetrahedron inscribed in this sphere, the experimental and the theoretical amplitudes of the deflections in the four leads could be compared. In general, it may be said that, with one exception, the deflections in the limb leads had the relative magnitudes expected. The deflections in the lead from the back were much smaller than anticipated. The last result is attributed to circumstances peculiar to the single experiment performed.

APPENDIX

Proposed Method of Finding the Spatial Electrical Axis.—The field of an electric dipole of moment M, located at the center, O, of a homogeneous conducting sphere of radius, R, is given by the equation

$$V_P = M \cos \theta \ (1/r^2 + 2r/R^3)$$

where V_P is the potential at the point P, r is the length of the line OP, and θ is the angle made by this line with the axis of the dipole. When P is on the surface of the sphere this equation reduces to

$$V_P = A \cos \theta \qquad \text{where } A = 3M/R^2.$$

It may be pointed out that cos θ of this equation is equal to the sum of the products formed by multiplying each of the direction cosines of the line OP by the corresponding direction cosine of the axis of the dipole.

Let R, L, F, and B be the apices of an equilateral tetrahedron inscribed within the sphere. Take the center of the sphere, O, as origin, and take as X axis the line parallel to RL, as Y axis the line parallel to the perpendicular bisector of RL which passes through F, and as Z axis the line OB. The lines from O to the apices of the tetrahedron will then have the direction cosines listed as follows:

	X AXIS	Y AXIS	Z AXIS
OR	$-\frac{1}{3}\sqrt{6}$	$-\frac{1}{3}\sqrt{2}$	$-\frac{1}{3}$
OL	$\frac{1}{3}\sqrt{6}$	$-\frac{1}{3}\sqrt{2}$	$-\frac{1}{3}$
OF	0	$\frac{2}{3}\sqrt{2}$	$-\frac{1}{3}$
OB	0	0	1

Let the axis of the dipole have the direction cosines a, b, and c. The potentials of the apices of the tetrahedron will then be given by the following equations:

$$
\begin{array}{llll}
V_R = A & (\ -\frac{1}{3}\sqrt{6}\ a & -\frac{1}{3}\sqrt{2}\ b & -\frac{1}{3}\ c\ ) \\
V_L = A & (\ \ \frac{1}{3}\sqrt{6}\ a & \frac{1}{3}\sqrt{2}\ b & -\frac{1}{3}\ c\ ) \\
V_F = A & (& \frac{2}{3}\sqrt{2}\ b & -\frac{1}{3}\ c\ ) \\
V_B = A & (& & 1\ c\ )
\end{array}
$$

The dipole may be regarded as the vector sum of two components, one of which is parallel to the plane defined by the points R, L, and F, and the other coincident with the line OB. The first of these components will have no effect upon the potential at B, and the second will have identical effects upon the potentials of R, L, and F. We may split A into two parts in the same way and define these two parts by the following equations:

$$
\begin{aligned}
A_f &= \sqrt{(Aa)^2 + (Ab)^2} \\
A_s &= Ac = V_B
\end{aligned}
$$

A_f bears the same relation to the first component of the dipole, and A_s the same relation to the second component, that A bears to the dipole itself. A_f may be expressed in terms of Einthoven's E derived from the potential differences between R, L, and F, regarded as the apices of the Einthoven triangle. We have

$$
\begin{aligned}
E^2 &= (V_L - V_R)^2 + \tfrac{1}{3}[(V_F - V_R) + (V_F - V_L)]^2 \\
(V_L - V_R) &= \tfrac{2}{3}\sqrt{6}\,Aa \\
(V_F - V_R) + (V_F - V_L) &= 2\sqrt{2}\,Ab
\end{aligned}
$$

Hence $E^2 = \frac{24}{9}[(Aa)^2 + (Ab)^2] = \frac{24}{9}(A_f)^2$ or $\frac{1}{4}\sqrt{6}\,E = A_f$

Since $A_s = V_B$, we have then

$$A = \sqrt{A_f^2 + A_s^2} = \sqrt{\tfrac{3}{8}E^2 + V_B^2}$$

The angle made by the axis of the dipole with the plane of RLF may be found by the formula, $\cot\beta = \frac{1}{4}\sqrt{6}\,E/V_B$.

It will be noted that $V_R + V_L + V_F + V_B = 0$ and if electrodes at the points R, L, F, and B are connected to a central terminal through equal resistances, this terminal will be at zero potential for all values of a, b, and c. The four leads

from the central terminal to the four electrodes will, therefore, record the potentials V_R, V_L, V_F, and V_B.

Let us suppose that the points *R*, *L*, and *F* are the apices of the triangle inscribed in the great circle represented by the intersection of the *XY* plane with the spherical surface, and that *B* is the point where the positive half of the Z axis penetrates this surface. The potentials of the four apices of the tetrahedron *RLFB* will then be given by the equations:

$$
\begin{aligned}
V_R &= A\,(-\tfrac{1}{2}\sqrt{3}a - \tfrac{1}{2}b)\\
V_L &= A\,(\tfrac{1}{2}\sqrt{3}a - \tfrac{1}{2}b)\\
V_F &= Ab\\
V_B &= Ac
\end{aligned}
$$

Here $V_R + V_L + V_F = 0$, $E/\sqrt{3} = A_f$, and $V_B = A_s = Ac$

$$A^2 = A_f^2 + A_s^2 = \tfrac{1}{3} E^2 + V_B^2 \text{ and } \cot \beta = (1/\sqrt{3})\,(E/V_B)$$

The potential at the apices of the tetrahedron are recorded by leading to the electrodes at its apices from a central terminal connected through equal resistances to the electrodes at *R*, *L*, and *F*, but not to the electrode at *B*.

Method of Computing the Effect of Varying the Resistance Between the Central Terminal and the Electrode at B.—If the potentials of the four electrodes at *R*, *L*, *F*, and *B* are V_R, V_L, V_F, and V_B, respectively, and the potential of the central terminal is V, we have for equal resistances, remembering that the sum of the currents meeting at a point is zero (Kirchkoff's second law).

$$
\begin{aligned}
&(V_R - V) + (V_L - V) + (V_F - V) + (V_B - V) = 0\\
&V = \tfrac{1}{4}\,(V_R + V_L + V_F + V_B)\\
\text{(a)}\quad &V_B - V = \tfrac{3}{4}\,V_B - \tfrac{1}{4}\,(V_R + V_L + V_F)
\end{aligned}
$$

When the resistance between the central terminal and the electrode at *B* is twice as large as the others we have

$$
\begin{aligned}
&(V_R - V) + (V_L - V) + (V_F - V) + \tfrac{1}{2}\,(V_B - V) = 0\\
&V_R + V_L + V_F + \tfrac{1}{2}\,V_B = \tfrac{7}{2}\,V\\
\text{(b)}\quad &V_B - V = \tfrac{6}{7}\,V_B - \tfrac{2}{7}\,(V_R + V_L + V_F)\\
&\tfrac{4}{3}\,\text{(a)} - \tfrac{7}{6}\,\text{(b)} = V_B - \tfrac{1}{3}\,(V_R + V_L + V_F)\\
&\text{(b)} = \tfrac{8}{7}\,\text{(a)} = \tfrac{6}{7}\,[V_B - \tfrac{1}{3}\,(V_R + V_L + V_F)]
\end{aligned}
$$

Note that $V_B - \tfrac{1}{3}\,(V_R + V_L + V_F)$ is the difference of potential between the central terminal and the electrode at *B* when the connection between the terminal and this electrode is broken and the other connections are left undisturbed.

REFERENCES

1. Lewis, T., and Rothschild, M. A.: The Excitatory Process in the Dog's Heart. Part II. The Ventricles, Phil. Trans. Roy. Soc., Lond. sB **206**:181, 1915.
2. Arrighi, Federico P.: El Eje Electrico del Corazon en el Espacio, Tesis del Doctorado en Medicina, Facultad de Ciencias Medicas, Universidad National de Buenos Aires, 1938.

ENDOCARDIAC ELECTROCARDIOGRAM OBTAINED BY HEART CATHETERIZATION IN THE MAN

ANTONIO BATTRO, M.D., AND HECTOR BIDOGGIA, M.D.
BUENOS AIRES, ARGENTINA

IN 1929 Forssmann,[1] after having his median basilic vein exposed by a surgeon, performed upon himself the first cardiac catheterization by introducing a ureteral catheter into the vein. This method has been used subsequently by several authors for various research purposes.

A year later Klein[2] determined the heart's minute volume in man, after Fick's principle, with venous blood obtained by catheterization of the right auricle. Similar determinations were carried out afterward in normal subjects by other authors.[3,4,20] Cournand and Ranges[6] described the technique of cardiac catheterization without exposure of a vein. Other hemodynamic investigations by means of cardiac catheterization have been carried out in pathologic conditions,[7-13] in the study of different drugs,[14,15] in septal defects of the heart,[16] and as a complement of radiologic examination.[17-19]

We have not found reports in the available literature of the application of this method to electrocardiographic studies. The endocardiac records which are mentioned in some papers have been obtained in animals by introduction of the electrodes into the veins of the neck or needles into the cardiac cavities through the walls of the heart.[21-24] It is the purpose of this paper to show the different electrocardiographic variations that are revealed by direct unipolar leads recorded within the chambers of the heart by cardiac catheterization.

The electrode placed inside the cardiac cavities functions as an active or exploring electrode and is in contact with the endocardial surface of the heart by means of the intracardiac blood. The term endocardiac electrogram means, therefore, an electrocardiogram obtained by a direct lead from the endocardial surface of the heart.

TECHNIQUE AND MATERIAL

We used a No. 8 ureteral catheter with a silver mandril inside and an electrode of the same metal 3 mm. long and 1.5 mm. wide at the tip. The catheter was introduced through the basilic vein up to the cardiac cavities, the position of the electrode being ascertained by radioscopic or x-ray examination.

From the Instituto de Investigaciones Físicas Aplicadas a la Patología Humana de la Academia Nacional de Medicina. "Donación Próspero Baurin." Sociedad de Beneficencia de la Capital. Sala de Cardiología del Hospital Rivadavia.

Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

To obtain the electrocardiograms we used a central terminal and connected the electrode of the left leg to the catheter. The records were made on Lead II. In this way the endocardiac electrode acted as an active exploring electrode. Connections were so arranged that when the exploring electrode became relatively positive, a positive deviation resulted in the tracing.

This procedure was used in twenty-three individuals (twelve normal subjects, two patients with left and one with right bundle branch block, two with ventricular extrasystoles, one with auricular fibrillation, one with auricular asynchronism and myocardial infarct, three with auriculoventricular dissociation, and one with Wolff-Parkinson-White syndrome). In some of these patients the procedure was repeated.

Standardization was 1 cm. per millivolt in auricular records and 2 mm. per millivolt in ventricular records.

AURICULAR ELECTROENDOCARDIOGRAM (ENDOCARDIAC P WAVE)

The electrocardiographic record of the auricular activity obtained by introduction of the electrode into the right atrial cavity is, in general, uniform. The auricular complex (P wave) begins sometimes with a slight downward deviation, 0.5 mm. or less in amplitude. An upward deviation of variable amplitude (from 2 to 12 mm.) follows, and, after this deflection, a new downstroke (4 to 20 mm.) is registered. From the ascending branch of the last negative deviation, generally at a point 2.5 to 7 mm. below the isoelectric level but occasionally from a point above this level, an upward wave begins which develops more slowly and is the beginning of the slow phase of the auricular complex. This wave rises 3 to 5 mm. above the isoelectric level and ends on a base line from which the ventricular complex begins. The duration of the auricular complex, thus considered, is 0.12 to 0.14 second.

The auricular complex consists, thus, of two parts: an initial rapid deflection, which is at first negative, then positive, then negative or first positive, then negative, and a slow part, which is generally negative in the first and positive in the second phase (Fig. 1). In order to facilitate the interpretation of these various deviations, we shall apply to them the letters used by Brown[25] in the esophageal electrocardiogram, with the exception of those used for the initial wave. Consequently S is assigned to the first negative deviation of the "endocardiac P wave"; *e* to the second positive deflection, *i* to the third negative deviation, *o* to the ascending branch of this wave, and *u* its final slow portion.

Comment.—

S Wave: We consider the first negative deflection S as the expression of the initial electric activity of the heart, activation of the sinoauricular node. It precedes the rapid auricular complex proper by approximately 0.02 second. This interpretation is supported by the fact that the nearer the catheter approaches the junction of the superior vena cava and the right auricle, a region close to the sinoauricular node, the larger and more distinct this wave becomes in successive records. The position of the catheter in relation to the sinoauricular node has been ascertained by x-ray examination. Another argument in favor

of our interpretation of the S wave is its agreement with Brown's interpretation[25] of the esophageal electrocardiogram and with the experiments of Wedd and Stroud[26] and of Eyster and Meek[27] referred to in Brown's paper. Brown has shown that when the esophageal catheter reaches the region near the left auricle, the activity of the sinoauricular node appears evident as a small negative wave (*s n*) which begins 0.011 to 0.018 second before the auricular complex *sensu stricto.** We have also observed this small negative S wave in esophageal electrocardiograms. Rijlant[28] has also succeeded in recording the sinus activity in man and in some mammals with a cathode oscillograph.

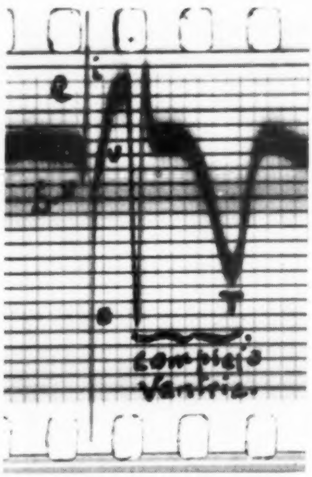
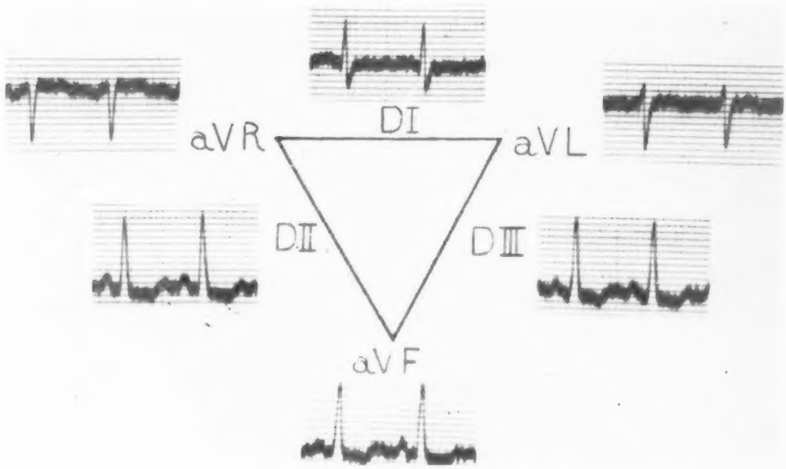


Fig. 1.—Endocardiac electrogram. Amplified tracing obtained with the electrode placed inside the right auricle. The auricular complex composed of S, *e*, *i*, *o*, and *u* waves and followed by its corresponding ventricular complex can be observed.

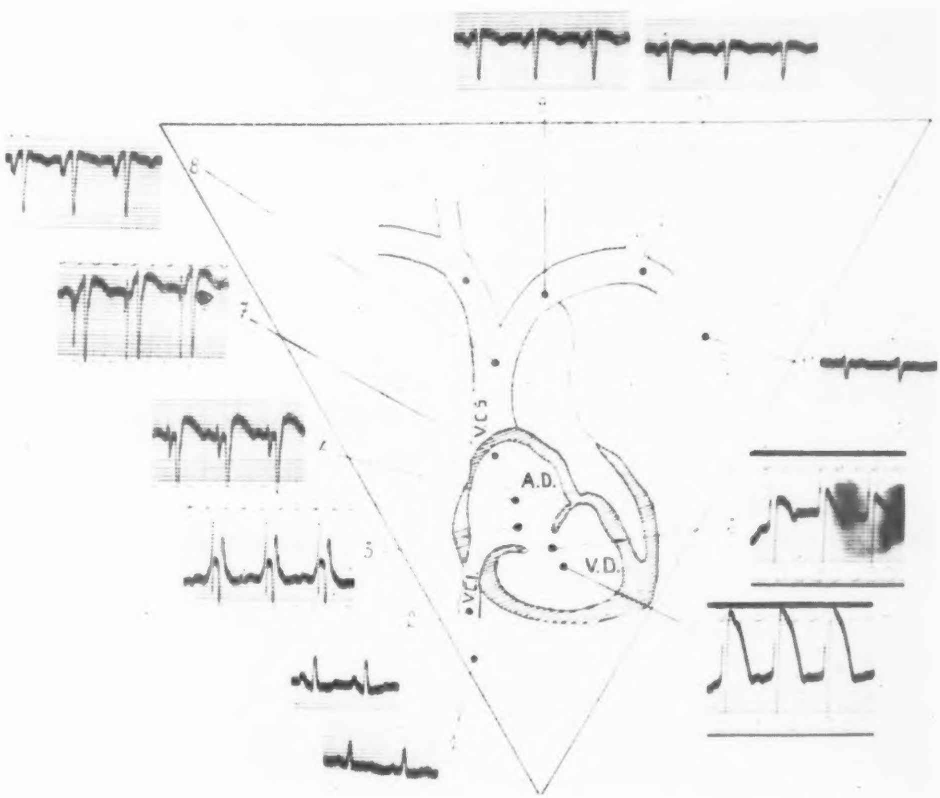
It is possible to explain the negativity of this S wave by the position of the electrode with relation to the sinus. Either the negativity of the endocardiac surface and of the auricular cavity close to it could be registered by the auricular electrode as a negative deflection or the electric potentials, when the sinus is activated, could move farther from the electrode and produce a negative deflection in the electrocardiogram. The S wave would thus represent the process of excitation of the sinoauricular node, inside which a wave of depolarization would also arise. Such a wave with the electrical axis pointed downward would sweep the node and radiate in all directions. It is not possible to trace this activity of the node in the other electrocardiographic leads since it affects these leads slightly.

The e, i, o Group of Waves: The rapid waves of the auricular complex, *e, i, o*, represent the activation of the atrial walls. The wave of excitation originating

*In referring to this paper we have purposely changed the direction of the waves, since the author registered the electropositivity of the esophageal electrode as a negative deflection and its negativity as a positive deviation, which is the inverse of the technique used in our work.



A.



B.

Fig. 2.—*A*, Electrocardiogram in Leads I, II, III, aVR, aVL, and aVF in a normal case. Heart in vertical position. *B*, Endocardiac electrogram of the same case obtained with the electrode placed at various points: right ventricle, right auricle, inferior vena cava, superior vena cava, innominate vein, and left subclavian vein. The catheter was introduced into the left arm. At the level of the superior vena cava and the innominate vein the record is similar to that of aVR; the record obtained in the left subclavian is similar to that obtained in aVL.

in the sinoauricular node spreads through the auricles in all directions and gives rise to a depolarizing wave parallel in direction to the walls of the auricles. In front of this depolarizing wave are the positive potentials of the regions not yet activated and behind it the negative potentials of those muscular fibers just excited.

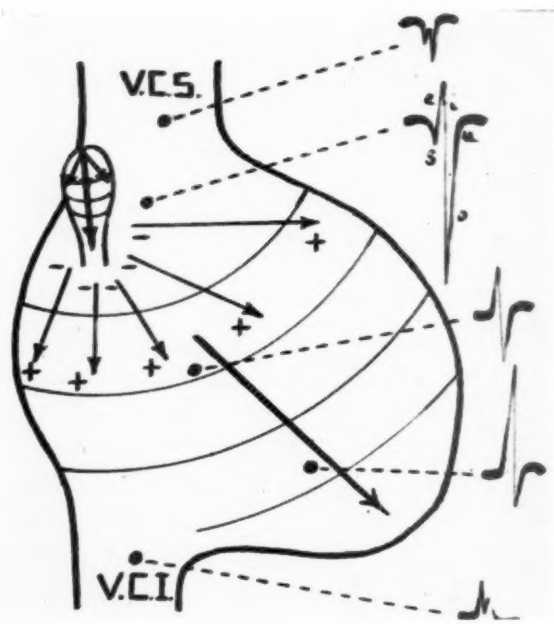


Fig. 3.—An outline of the auricular complex as recorded at different levels.

These electrical potentials influence the endocardiac electrode, the form and amplitude of the waves registered varying according to the situation of the electrode (high, medial, or deep) inside the atrium (Fig. 2). When the endocardiac electrode is placed in the upper portion of the atrium, the excitation waves approaching it produce a small positive *e* deviation, and those waves moving away cause a large negative *i* deviation because of the fact that the portion of the auricular myocardium above the electrode is relatively small and the portion below it is much larger. The reverse happens when the electrode is placed low in the auricular cavity; the depolarizing waves approaching the electrode (big *e* deviation) predominate over those waves moving away (small *i* wave). The potentials which approach and withdraw from the electrode become equilibrated when the electrode is placed in an intermediate position which results in *e* and *i* waves of equal amplitude (Fig. 3).

These endocardiac depolarizing waves are similar to the *e*, *i*, *o* waves of the esophageal electrocardiogram. Brown considers the *i* wave as the "intrinsic" wave, which, according to the conception of Lewis and associates,[29] is the deviation representing the activation of the small muscular area in contact with the

electrode. Lewis and associates observed that the intrinsic wave, which indicates the arrival of the excitation wave under the esophageal electrode, is recorded at variable intervals in relation to the P wave of the auricular complex in standard leads.

In the endocardiac electrocardiogram the *i* wave represents also the "intrinsic" wave of auricular activity. Its appearance indicates that the depolarizing wave has reached the electrode and has gone on its way to more distant regions. The *o* deflection shows the activation of the last portions of the auricle and ends when the impulse has spread throughout the auricular wall. At this moment depolarization is complete. The rapid complex *e, i, o* measures from 0.04 to 0.08 second. The auricular endocardiac electrocardiogram, therefore, registers the intrinsic wave which is preceded and followed by extrinsic waves, the latter representing the activation of auricular regions distant from the endocardiac electrode.

The *o-u* segment and *u* wave represent the repolarizing process of the auricles and are similar to the junction point, J, and S-T segment of the ventricular complex. The positive or negative deviations of this segment are due to an acceleration of the repolarizing process caused by tachycardia which generally accompanies the catheterization. The acceleration of cardiac rate in normal conditions can also cause an alteration at the J junction and S-T segment of the ventricular complex. There are cases in which the *o-u* segment is absent and group *e, i, o* ends in a horizontal line which represents the passage of the impulse through the auriculoventricular node.

Ta Wave: In our patients with sinus rhythm, the ventricular complex interfered with the slow waves of the auricular complex. We have been unable, therefore, to differentiate the T wave pointed out by Hering,[30] (Ta wave), produced by the auricular activity. However, it was possible in one case of A-V block to record this part of the auricular complex which, as a whole, is similar to the ventricular complex. In this particular case a 2 mm. downstroke which we identify as a Ta wave can be observed immediately after the *u* slow deflection (Figs. 4 and 5). This Ta wave represents the final phase of repolarization of the atria.

The total duration of the auricular activity (P + Ta) is 0.60 second. This final wave (Ta wave) of the auricular complex has been demonstrated in man in esophageal electrocardiograms by Boden and Neukirch[31] and by Sprague and White[32] in A-V dissociation and auricular extrasystoles.

In standard and esophageal leads the direction of Ta is opposite to that of the P wave. In most cases with an upward P wave, the Ta wave is directed downward. When P appears inverted, Ta is positive. When the depolarizing and repolarizing waves have different directions, the deflections which represent these phases in the electrocardiogram are concordant, as happens normally in the ventricles (R and T waves, respectively). At the level of the auricles the depolarizing and repolarizing waves have the same direction which results in a discordant inscription in the electrocardiogram: a positive P and negative Ta.

According to Sprague and White[32] the interval P + Ta measures 0.34 to 0.42 second and the relation $\frac{P + Ta}{P}$ is 3.7 seconds on the average. Brown[25] gives higher figures: 0.405 to 0.503 second and 4.7 seconds, respectively. In our case the interval P + Ta was 0.60 second and the relation $\frac{P + Ta}{P}$ was 5 seconds, as mentioned previously.

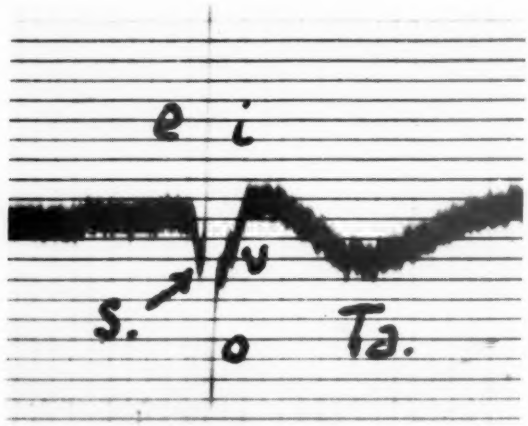


Fig. 4.—Amplified auricular electrogram. The auricular complex consists of two phases: a rapid initial part (S, *e*, *i*, and *o* deviations) and a slow final part (Ta wave). The initial negative S deviation indicated by the arrow corresponds to the excitation of the sinoauricular node.

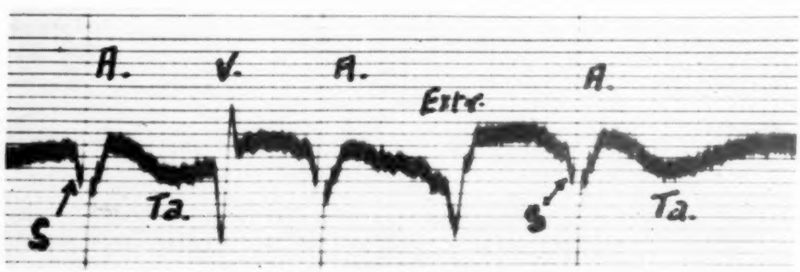


Fig. 5.—Endocardiac electrogram in a case of auriculoventricular dissociation (electrode in the right auricle). It can be observed that auricular activity, *A*, is independent of ventricular activity, *V*. Among the last auricular complexes, a ventricular extrasystole appears. The auricular complex shows the characteristics of its sinus origin.

The proper differentiation of the Ta wave is important in diagnosis because, being a negative deflection, it can be traced in standard leads as a depression of the S-T segment and is likely to be regarded as an abnormality of the ventricular complex. The participation of this wave in the QRS group of the ventricular activity is easily explained by the long P-Ta interval.

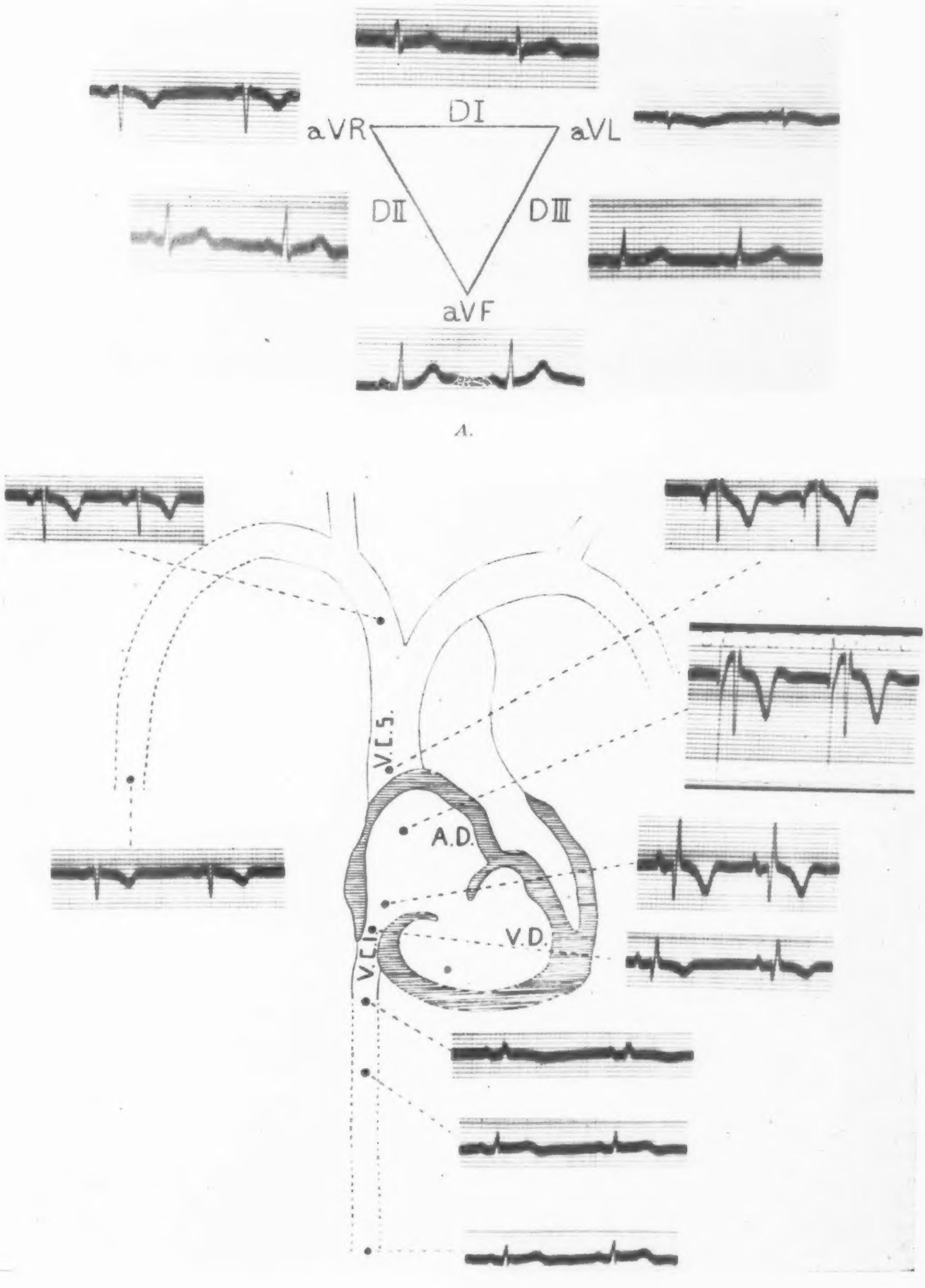


Fig. 6.—*A*, Electrocardiogram in Leads I, II, III, aVR, aVL, and aVF. Heart of vertical type. *B*, Endocardiac and endovascular electrograms. The auricular endocardiac electrogram shows the variations of auricular and ventricular endocardiac potentials according to the position of the electrode, high and low inside the auricle and in relation to the auriculoventricular orifice.

As the electrode descends into the inferior vena cava, the electrogram resembles the aVF lead. Conversely, as the electrode is successively placed into the superior vena cava and in the subclavian and right humeral vein, the electrogram becomes similar to one obtained in aVR.

The P-R segment is frequently observed to have a negative deviation in standard leads. Considering the time of its production in relation to the inscription of the ventricular complex, we feel that it corresponds to the *o-u* segment of the auricular complex rather than to the Ta wave.

As the catheter is progressively withdrawn from the auricular cavity into the superior vena cava, the shape of the auricular complex undergoes a corresponding modification (Figs. 2,*B* and 6). First the rapid waves (intrinsic and extrinsic waves) disappear; then the auricular complex begins to acquire more and more the appearance of auricular waves in standard leads or in unipolar limb leads, while the *o-u* segment disappears. When the catheter is in the superior vena cava, the P wave usually is negative, of great amplitude, and sharply pointed. In spite of its larger amplitude, it resembles a P wave recorded in aVR leads (Fig. 7,*B*).

The successive modifications of the auricular complex observed in our studies confirm the findings of Lewis and Rothschild[33] in animals. When their records were taken with the electrode inside the superior or inferior vena cava, a region where these great vessels are surrounded by auricular muscle, they observed disappearance of the intrinsic deflection and the sharp deviations of the auricular endocardiac electrocardiogram.

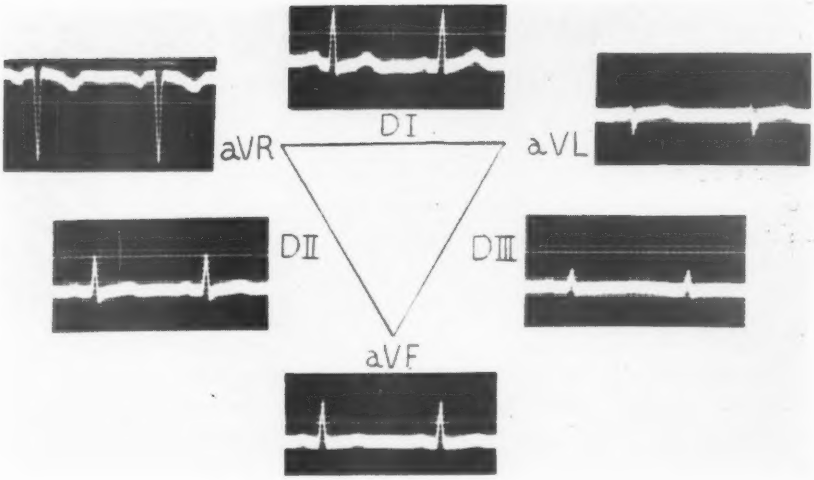
When the records were taken in the innominate vein, the P wave was similar in shape to that of the aVR lead. The same was observed if the electrode was placed in the right subclavian vein or at the level of the right basilic vein. In one case in which the catheter was introduced on the left side, the P wave maintained its negativity in the vein of the left arm although the same P wave in the aVL lead appeared positive (Fig. 7).

By taking successive records from positions between the interior of the heart and the peripheral vessels, variations from an endocardiac P to a P wave characteristic of the standard limb leads can be obtained.

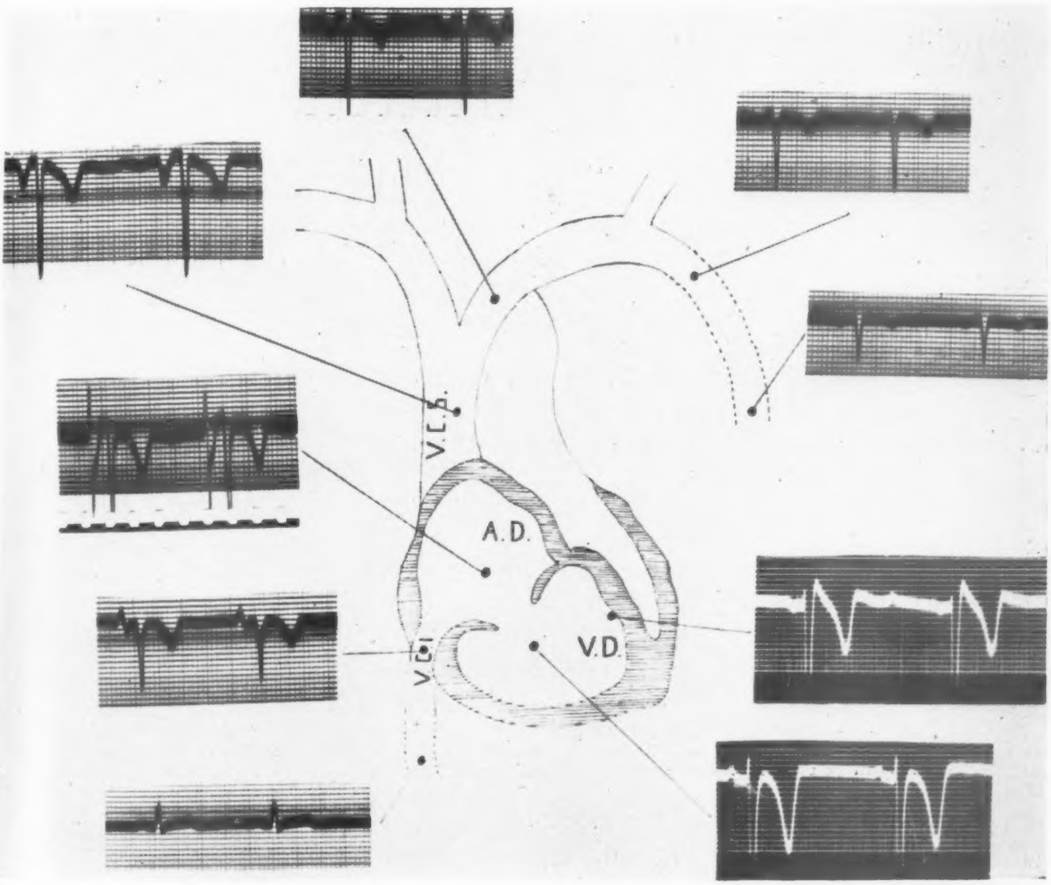
The shape shown by the P wave in standard or limb leads results from the numerous electrical influences that effect the auricular wall and from the difference in the conductivity of the tissues for the potentials produced by auricular contraction. The negativity of P in leads taken from the superior vena cava and from the innominate vein is accounted for by the position of the electrode in relation to the direction of the wave of depolarization of the auricles, which radiates from the sinus node and spreads through the auricular wall away from the exploring electrode. Under these circumstances the auricular electrocardiogram behaves as it does in semidirect leads.

In summary, it can be said that the auricular electroendogram behaves as a direct endocardiac lead and in certain aspects resembles the auricular portion of the esophageal electrocardiogram obtained at the level of the auricles. It consists of a series of initial rapid deflections (S, *e*, *i*, *o* waves) joined to a final slow and negative portion (Ta wave) by a frequently deviated *o-u* segment.

The first negative deflection (S wave), which cannot be registered always is considered to be the result of activation of the sinoauricular node. The rapid deflections (*e*, *i*, *o* waves) constitute the intrinsic and extrinsic waves of the auricular depolarization process, while the final slow wave (Ta) represents the



A.



B.

Fig. 7.—*A*, Electrocardiogram in Leads I, II, III, aVR, aVL, and aVF in a normal case. *B*, Electrograms of the same case with the electrode in different situations. Catheter introduced by the left side. At the level of the inferior vena cava the electrogram is similar to aVL. At the level of the superior vena cava and innominate vein it is similar to aVR. At the level of the left humeral vein a negative T wave still persists. At the level of the auricle, the auricular and ventricular complexes are distinctly shown. At the level of the ventricle, the auricular complex is similar to that of the standard leads.

The ventricular complex shows the characteristics of the endocardiac ventricular electrogram of type I.

repolarization process. At the level of the superior vena cava the endocardiac auricular electrocardiogram loses its endocardiac characteristics and resembles that obtained in semidirect leads (similar negative P wave but of greater amplitude than the P observed in the aVR lead).

VENTRICULAR ENDOCARDIAC ELECTROGRAM

The ventricular endocardiac electrogram can be recorded from inside either the ventricular or the auricular cavity (types I and II, respectively).

Type I Ventricular Endocardiac Electrogram.—With the electrode placed inside the ventricle, the electrocardiogram shows a rapid deflection followed by a slow one (Figs. 2,*B*, 7, and 8). The first deflection consists of three phases:

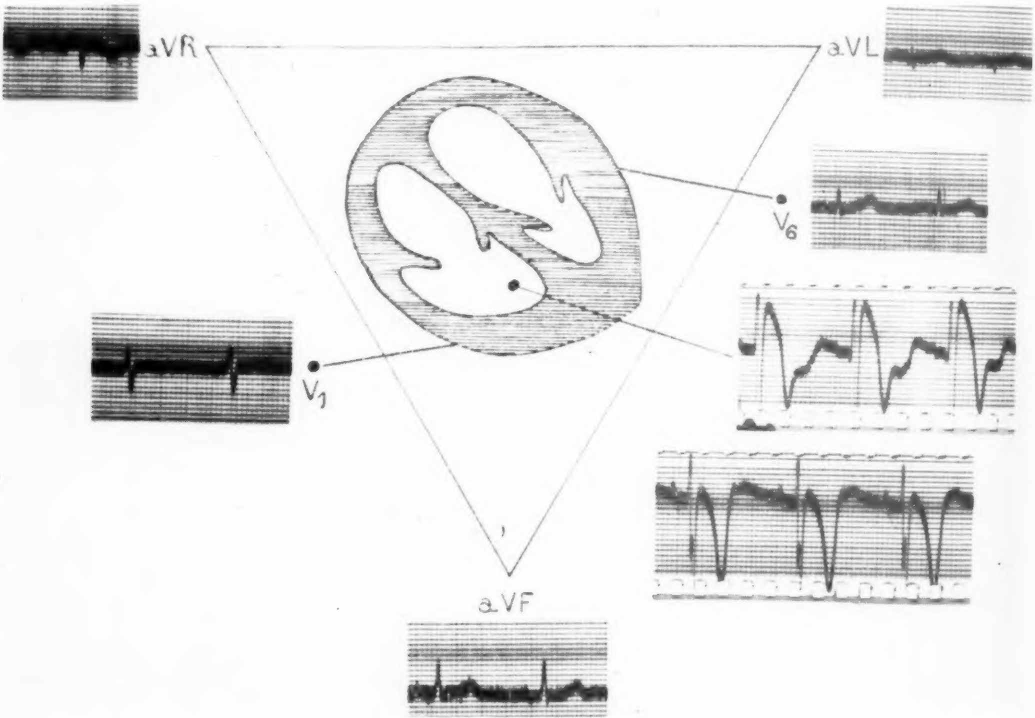


Fig. 8.—Ventricular endocardiac electrogram. A record obtained with the catheter placed in the right ventricle. Variations in the shape of the ventricular complex according to the depth of the catheter can be observed. Precordial electrocardiogram made at Positions 1 and 6 (V_1 and V_6).

an initial upward R wave, a downward S wave, and a third upward inconstant wave, R′. The amplitude of the initial positive stroke varies from 1 to 10 millimeters. The negative stroke has a greater amplitude (from 15 to 20 millimeters). The third positive wave may extend as much as 20 mm. above the isoelectric level. In the same record, however, it may end on the isoelectric line if the position of the catheter inside the ventricle is modified.

The slow wave (T wave) begins generally above the isoelectric level or, less frequently, on the isoelectric line, and describes a curve with an upward and outward convexity. When the slow deflection begins on the isoelectric line, the deviation ends as a large, sharp, and deeply negative wave. When it begins above the isoelectric line, it may go considerably below the isoelectric line or it may stop at this line.

QRS Group: When the catheter is placed in the ventricular cavity, the ventricular complex has, as we have seen, an initial positive deflection (R wave), followed by a negative deflection of great amplitude (S wave). We consider the first deflection (R wave) to be the result of the excitation of the interventricular septum.

According to Ashman and Hull,[34] "the interventricular septum is excited on both sides almost simultaneously. However, as the left branch divides immediately below the His bundle the area of depolarization may be at first probably greater and anticipated in the left side of the septum than in the right side." The electrical axis of this depolarizing wave points then from left to right and is not "counterbalanced" by the depolarization of the right side of the septum which has not yet begun.

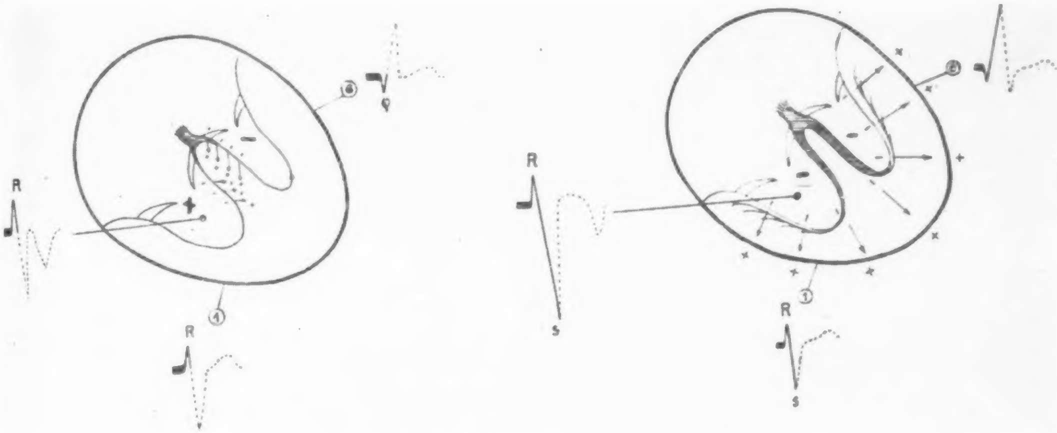


Fig. 9.—An outline of potential variations of the endocardiac electrode and of precordial leads made at Positions 1 and 6 at different moments of the process of cardiac excitation (see text).

The waves of excitation of the superior portion of the septum, therefore, travel from left to right; that is, they approach the endocardiac electrode and produce the first positive deflection (R wave). In precordial leads this initial activity of the septum is represented by a small initial R wave at Position 1 and by a Q wave at Position 6 (Fig. 9). In fact, when the septum is thus activated, the left ventricular cavity has from the first moment a negative potential and an electrode placed on its surface (Position 6) registers this negativity through the ventricular wall, which is as yet inactivated. A negative deflection, a true septal Q wave, will thus result at points over the surface of the left ventricle.

In its turn the right ventricular cavity will be in the positive field of the excitation wave. Both the endocardiac electrode and an electrode placed over the surface of the right ventricle (Position 1) will record its positivity. Of course a precordial electrode at Position 1 will in its turn be influenced (approximately 0.025 second after) by the activation of the right ventricular wall, the depolarization wave of which, with its positive field displayed forward, advances toward the precordial electrode at points over the surface of the right ventricle, and contributes in this way to the production of the small, initial positive wave.

If this interpretation is correct, the initial positive deflection (R wave) will be absent in an endocardiac electrocardiogram in cases of left branch block because the direction of the depolarization electromotive force of the septum in this case is from right to left. It will be shown later that an R wave does not appear when left bundle branch block is present.

The following negative deflection (S wave) may be considered to represent the negativity of the ventricular cavity at the precise moment that the ventricular complex is registered. Once the septum has been depolarized, the impulse continues to activate the ventricular wall from the endocardiac toward the subpericardiac regions. First the anterior surface of the right ventricle near the interventricular septum is excited, then the excitation reaches the lateral portion of the right and the left ventricles, and finally the base and pulmonary conus of the right ventricle are excited.[34]

Throughout all this process, due to the direction of the depolarizing electromotive force in the ventricular walls, an electric field is generated which is relatively negative in the endocardiac surface and the ventricular cavity and relatively positive at the crest of the excitation wave as it moves toward the epicardium (Fig. 9).

The endocardiac electrode placed inside the ventricle is thus in a negative field, a circumstance revealed by a large downward deviation (S wave). The excitation waves both from the right and the left ventricles, moving away from the electrode, account for the great amplitude of this deflection. In other words, the electrode registers the negative potential of the right ventricular cavity plus that of the left ventricle transmitted through the interventricular septum which, at the moment, is in a state of complete depolarization. The depolarization of the left ventricle is not completed until a little later because of the greater size and thickness of its wall. The complete depolarization of the ventricular walls coincides with the commencement of the ascending branch of the S wave which sometimes reaches the isoelectric level when depolarization is complete.

If an electrode is placed on the pericardium, Position 1, at the moment the S wave is recorded in a precordial electrocardiogram, it will detect the potentials moving away from it which results in the inscription of a negative deviation (S wave). Conversely, if the electrode is placed at Position 6, it will detect the approaching potentials of the left ventricular wall and consequently an upward positive deflection will be inscribed (R wave).

Endocardiac Ventricular T Wave: This wave is definitely negative, sharp, and deep (Figs. 1, 2,*B*, 7, and 8), both when recorded with the electrode inside the ventricle or inside the right auricle. It has thus the same direction as the ventricular wave of greatest amplitude. To explain the negativity of this wave it has been assumed that either the repolarization of the ventricular walls begins in the subepicardial region or that the velocity of repolarization is greater in the subepicardial than in the endocardial area.[34] The endocardiac electrode is thus placed in the negative field of the wave of regression and a downward deflection (negative T wave) is inscribed. This deflection has great amplitude because it is caused by the negative potentials of both the left and the right ventricles.

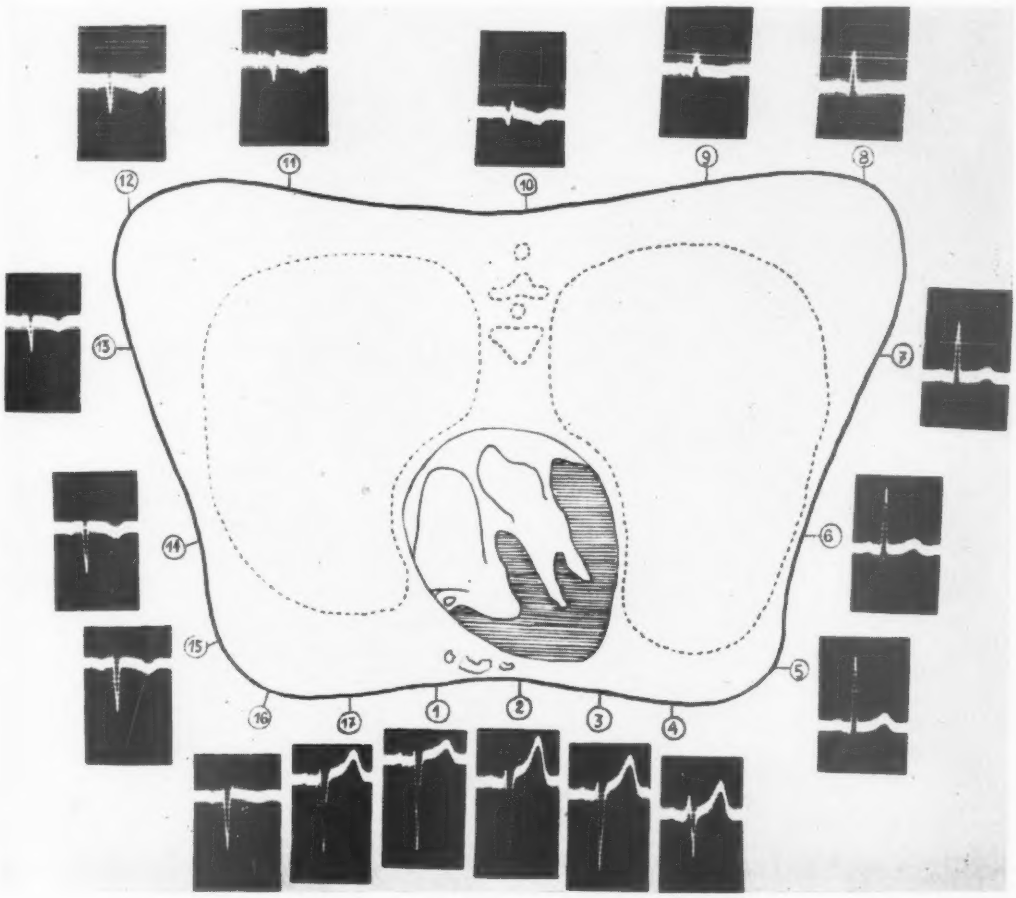


Fig. 10.—Unipolar electrocardiograms obtained from points around the thorax. This tracing belongs to the same subject whose tracings are shown in Fig. 7.

When placed at points on the precordial surface over either the left or the right ventricle, the electrode is in the positive field of the repolarization wave and consequently records an upward deflection (positive T wave).

At precordial Positions 10 to 16, T is recorded as a negative deflection because in this region the ventricular wall has little or no influence, and the electrode is directly influenced by the negativity of the ventricular cavity (Fig. 10).

S-T Segment: The S-T segment of the ventricular electroendocardiogram frequently begins above the isoelectric level. Our tracings indicate that the more deeply the catheter is introduced into the ventricle, that is, the closer the electrode is to the interventricular septum, the greater is its positive deviation. The initial positive deviation of the S-T segment seems to be due, therefore, to the repolarization of the interventricular septum, while the T wave is produced by the repolarization of the free walls of the ventricles. Pardee and Goldenberg[35] proved that deviation of the S-T segment was more frequent in cases of infarcts affecting the interventricular septum. Deviation of the S-T segment might also be related to the position of the electrode in the ventricular cavity, its inscription being determined simply by the contact of the electrode against any point of the ventricular wall.

Type II Endocardiac Ventricular Electrogram.—The ventricular electroendocardiogram (Fig. 11) maintains its characteristics even if recorded with the catheter placed inside the right auricle, the only difference in this case being that the initial R wave disappears or is of small amplitude. This peculiarity supports the theory that the initial positive wave of the ventricular electroendocardiogram represents the activation of the septum, since when the catheter is in the auricle it is at a greater distance from the septum and is less influenced by its activation.

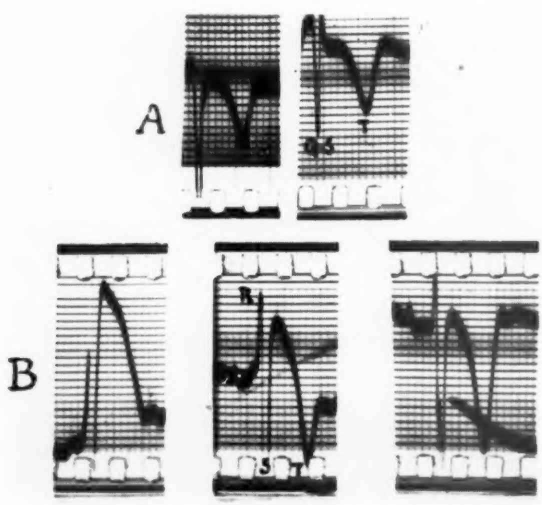


Fig. 11.—Ventricular endocardiac electrograms of types I and II.

When placed in the auricle the electrode detects the negative potentials of the ventricular cavity through the auriculoventricular orifice of the tricuspid valve. Thus, a negative QS deviation and a negative T wave result.

When the catheter is near the A-V opening, it registers a final positive deviation (R′), which disappears when the catheter is withdrawn a little. This R′ wave represents the activation of the remaining portions of the ventricles, probably the basal region of the right ventricle and the conus of the pulmonary

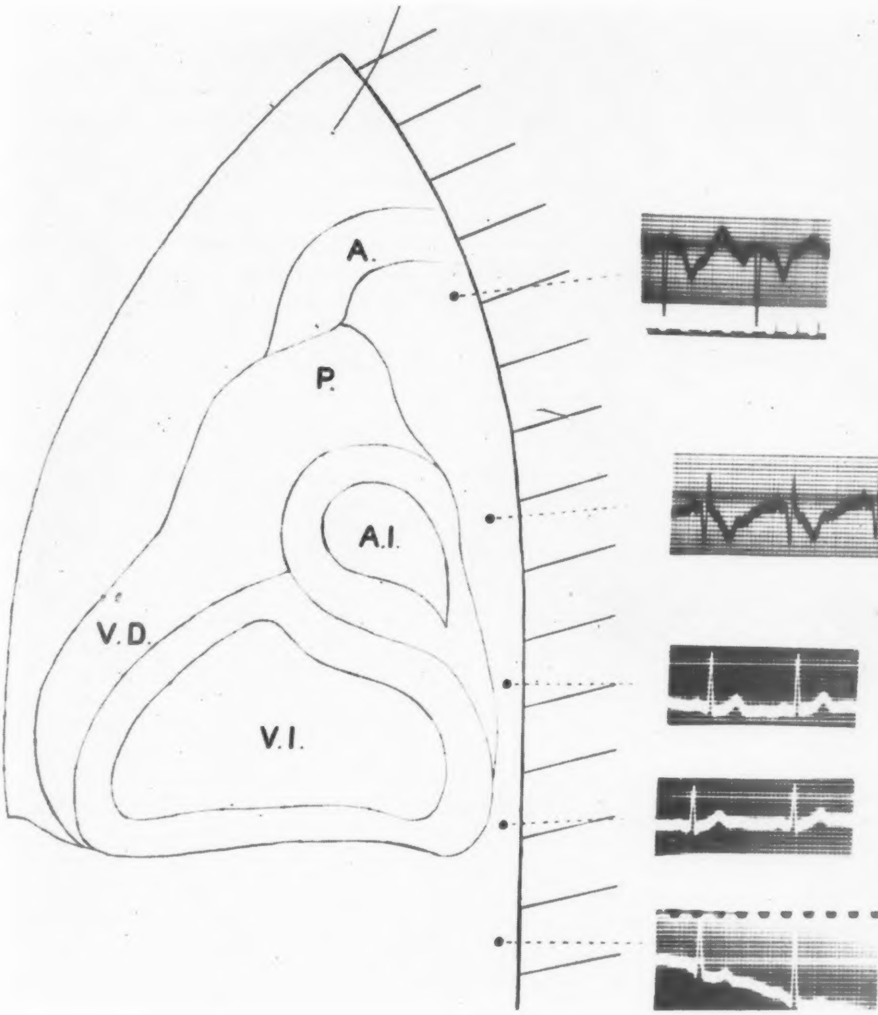


Fig. 12.—Esophageal electrocardiogram at different heights. The esophageal electrocardiogram obtained at the level of the auricle (the second tracing from the top) is similar to the ventricular electrogram obtained with the catheter in the right auricle (type II endocardiac electrogram).

artery. When these zones become excited, the electromotive forces advance toward the electrode placed in the neighborhood and a positive wave will be recorded. This positive deflection has been regarded as the equivalent of the S wave of the precordial electrocardiogram taken at Positions 5 and 6. Such

an interpretation is supported by the observation of a positive final wave in the electroendocardiogram in one case which showed the S wave in tracings taken from Positions 5 and 6. In another case with no S wave in tracings made at Positions 5 and 6, such a deflection was not observed. This type of endocardiac electrocardiogram is similar to the esophageal electrocardiogram recorded at the level of the auricle (Fig. 12).

VENTRICULAR ENDOCARDIAC ELECTROGRAM RECORDED FROM THE VENA CAVA

In records obtained with the electrode placed in the superior vena cava, the ventricular complex has the same characteristics as the ventricular endocardiac electrogram recorded from the auricular cavity except that its amplitude is often less. Its shape also resembles the shape in Lead aVR since an electrode placed in the superior vena cava and an electrode placed on the right arm both have almost the same relation to the valvular openings at the base of the heart. In both cases negativity of the ventricular cavity during the recording of the QRS group of waves is registered. The endovascular electrogram maintains these characteristics (shown in Fig. 6) when taken at the level of the subclavian vein or the veins of the right arm.

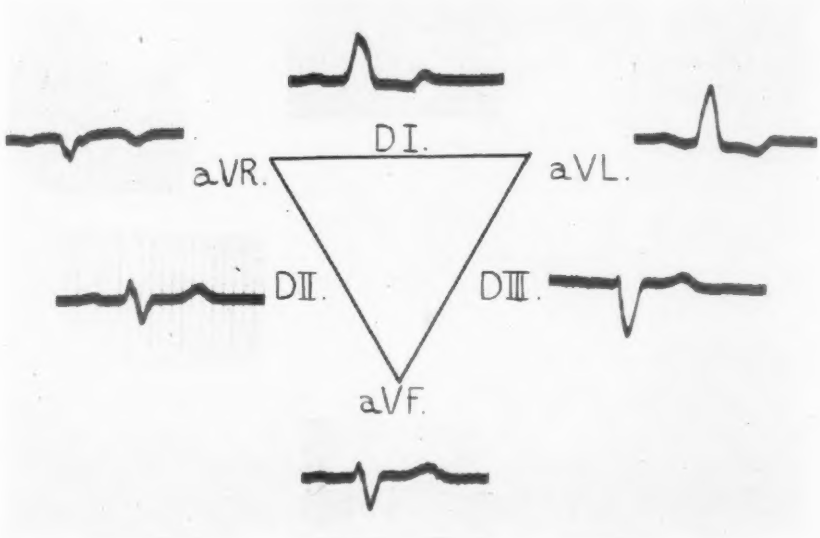
The pattern of the electrogram made with an electrode at the level of the inferior vena cava is similar to the pattern observed in Lead aVF (Figs. 6 and 7). This confirms the observations of Helm and associates[36] concerning the distribution of ventricular potentials below the diaphragm. These authors demonstrated that the diaphragmatic type of electrocardiogram is obtained when the variations of potentials are registered from the left leg as well as from the anterior or posterior surface of the abdomen below the diaphragm (upper intestines or duodenum).

VENTRICULAR ELECTROENDOCARDIOGRAM IN LEFT BUNDLE BRANCH BLOCK

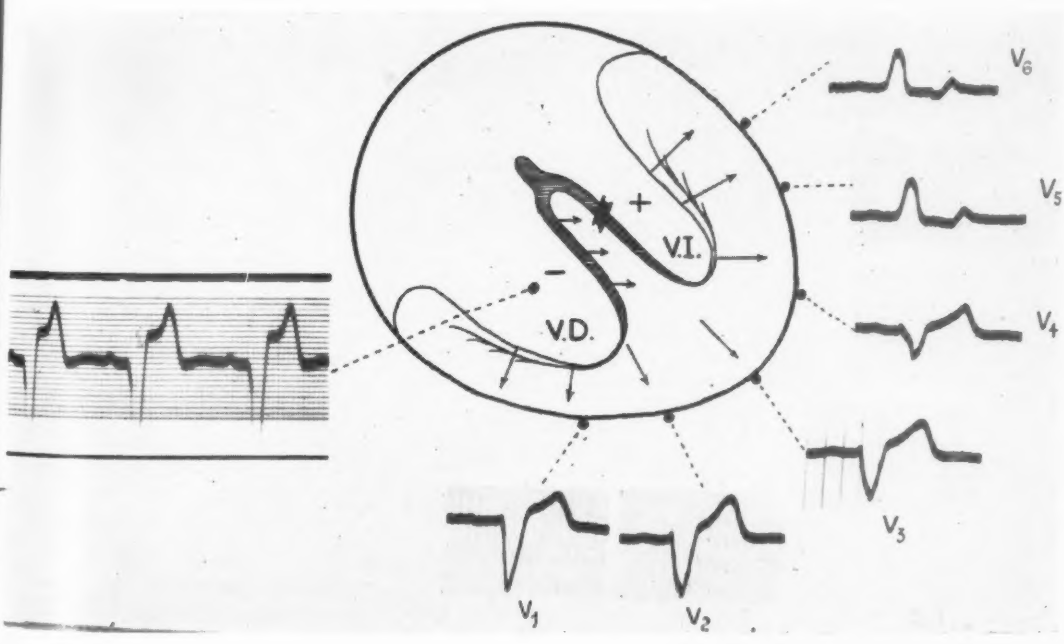
In our cases of left bundle branch block (Fig. 13) the ventricular electrocardiogram recorded with the electrode inside the right ventricle shows no initial positive wave and consists of a simple downward deflection of great amplitude followed by an S-T segment with a positive deviation and a positive T wave.

The shape of this record is similar to the ventricular endocardiac records obtained in animals by Wilson and associates[37] after section of the left branch of the bundle of His (Fig. 14). It is also similar to the electroendocardiogram obtained by the same authors from the left ventricular cavity after section of the right branch of the bundle of His (Fig. 17).

The similarity of our tracings to those registered in precordial leads taken at points over the right ventricle is evident (Fig. 13,*B*).



A.



B.

Fig. 13.—Bundle branch block, common type. ***A*, Electrocardiogram in Leads I, II, and III and in unipolar limb leads. In aVR the ventricular complex is negative. Heart in horizontal position. *B*, Precordial leads and ventricular endocardiac electrogram of the same case (electrode inside the right ventricle) (see text).**

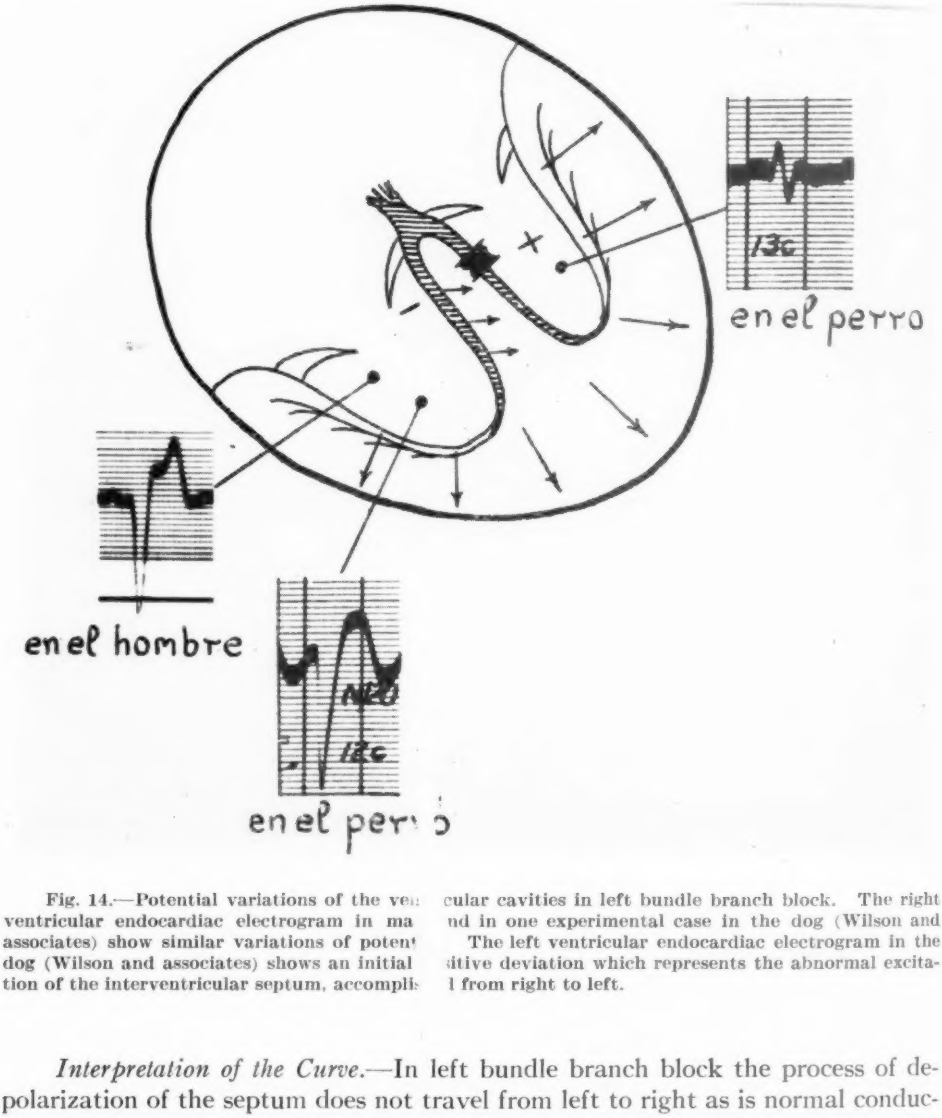


Fig. 14.—Potential variations of the ve cular cavities in left bundle branch block. The right ventricular endocardiac electrogram in ma nd in one experimental case in the dog (Wilson and associates) show similar variations of poten The left ventricular endocardiac electrogram in the dog (Wilson and associates) shows an initial itive deviation which represents the abnormal excitation of the interventricular septum, accompli l from right to left.

Interpretation of the Curve.—In left bundle branch block the process of depolarization of the septum does not travel from left to right as is normal conduction, but from right to left. The right ventricular cavity, therefore, remains negative from the beginning to the end of the inscription of the ventricular complex. This explains the change in shape of the ventricular wave to a negative deflection and the absence of the positive initial phase observed in normal cases. Were it possible to put the catheter into the left ventricular cavity of man, as Wilson[37] did in dogs, the tracings would show an initial positive phase produced by the spread of the impulse from right to left through the septum.

The peculiar shape of our ventricular electroendocardiogram confirms what has been observed in experimental bundle block. In left bundle branch block something similar to what happens in cases of extrasystoles of the right ventricle

can be observed (Fig. 15): the impulse starts from a focus in the right ventricle and travels to the left ventricle through the interventricular septum. A negative potential is thus produced in the cavity of the right ventricle. We have been able to record this negative potential in one case of left bundle branch block by introducing the electrode into the right auricle.

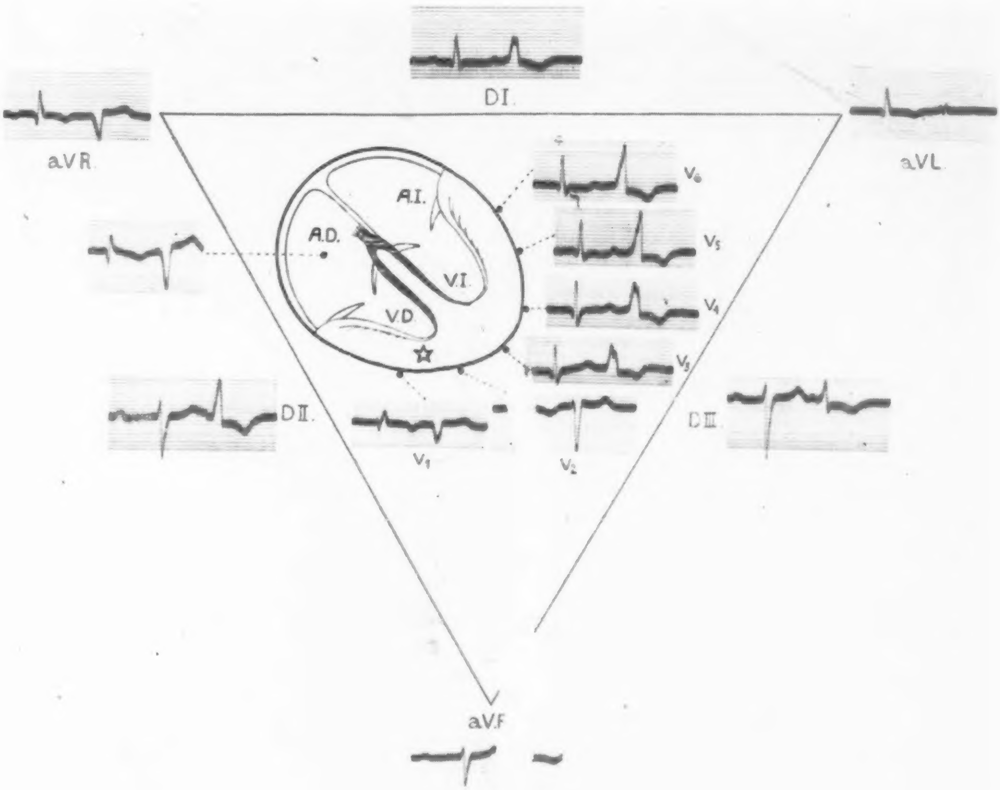
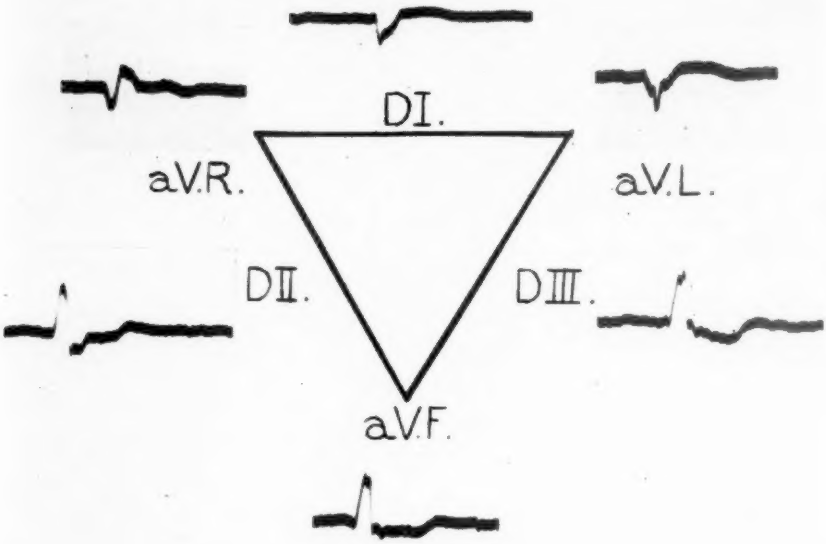


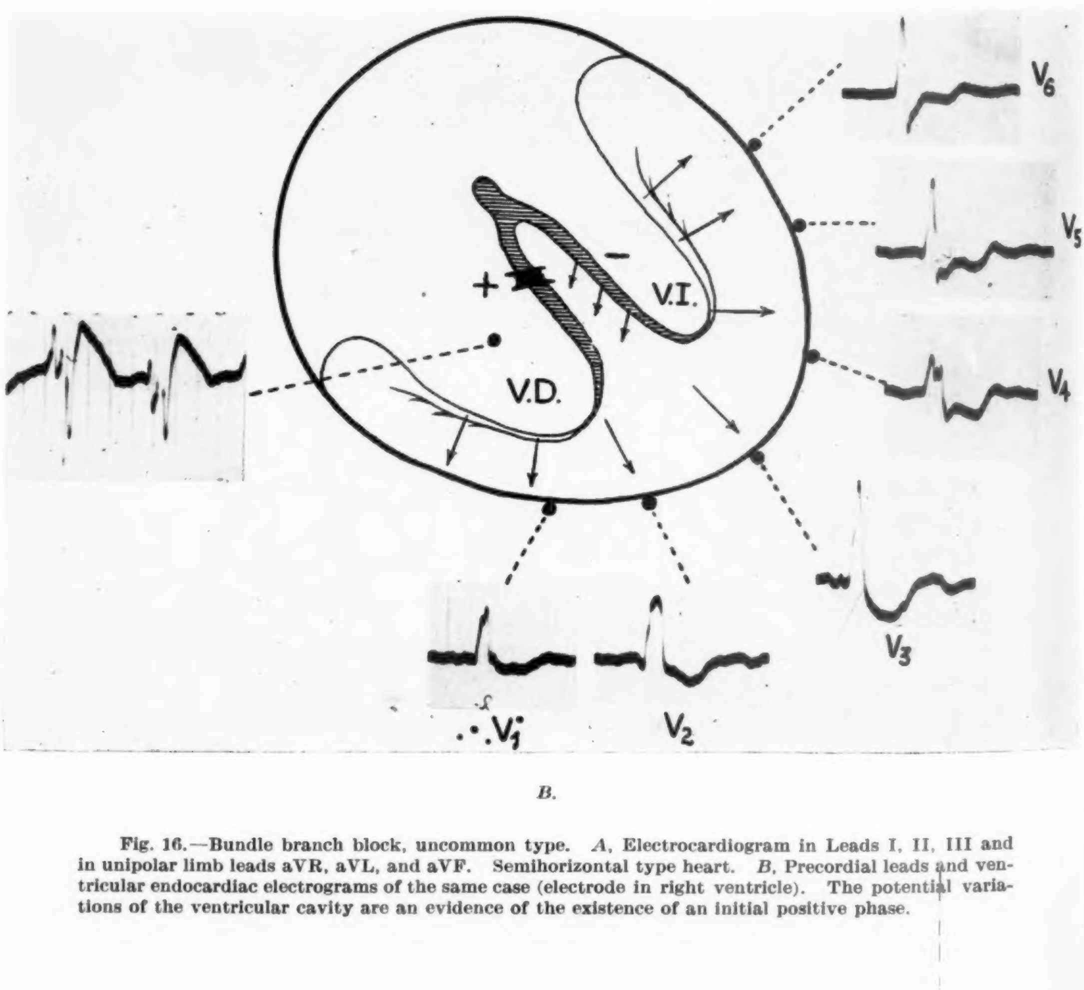
Fig. 15.—Electrocardiogram in standard leads, aVR, aVL, and aVF, and precordial and endocardiac leads in a case of right ventricular extrasystoles. (Electrode in the right auricle.) Heart in semihorizontal position. The extrasystolic complex detected in the auricle has a shape similar to that obtained in aVR and in the leads to the right of the precordial region.

The similarity of the findings in the ventricular endocardiac tracing to the findings in precordial leads made at points to the right and in the right arm lead (aVR) is easy to understand because in both types of tracing the negative potential of the right ventricular cavity is recorded. In precordial leads made from points on the left side and in the left arm lead (aVL), the electrode is placed in the positive field and the direction of the wave of activation is toward the left arm. Consequently a positive deflection results.

In brief, in cases of left bundle branch block, the electroendocardiogram is similar to the tracings obtained in right ventricular extrasystoles. This fact is



A.



B.

Fig. 16.—Bundle branch block, uncommon type. *A*, **Electrocardiogram in Leads I, II, III and in unipolar limb leads aVR, aVL, and aVF. Semihorizontal type heart.** *B*, **Precordial leads and ventricular endocardiac electrograms of the same case (electrode in right ventricle). The potential variations of the ventricular cavity are an evidence of the existence of an initial positive phase.**

further proof of the accuracy of the modern conception of the origin of left bundle branch block and of ventricular extrasystoles and of the relation of left bundle branch block, particularily, to the electrocardiogram which has been pointed out by one of us (Battro, in collaboration with Braun Menéndez and Orías[38]) and which is now generally accepted. According to this conception, those tracings which show the characteristics of bundle block and which have a positive deflection in Lead I should be considered to be the result of left bundle branch block.

It is not our purpose to discuss here whether or not there exists in these cases an anatomic lesion localized on the left side of the septum which interrupts the continuity of the bundle of His, a question which has recently been studied by Glomset and associates.[39] In any event it can be accepted that tracings which show the characteristics of left bundle branch block, whichever its etiology may be, indicate that in a given case the right ventricle receives the impulse and contracts sooner than the left ventricle.

VENTRICULAR ELECTROENDOCARDIOGRAM IN RIGHT BUNDLE BRANCH BLOCK

In the case of right bundle branch block which we have studied (Fig. 16), the electroendocardiogram taken from the right ventricle shows an upward deflection followed by a downward deflection which is of larger amplitude and notched. The S-T segment shows a positive deviation and is the point of origin of the slow wave corresponding to the period of repolarization (T wave). The T wave ends at the level of the isoelectric line or below it.

The tracing represents the phenomena occurring in the ventricular cavity and the underlying muscle, while the ventricular activity is registered. The right branch being blocked, the supraventricular impulse spreads along the left branch. This results in an activation of the interventricular septum from left to right. In this initial period of activation, the right ventricular cavity will be positive in relation to the left, in accordance with the orientation and direction of the electromotive force existing at the moment. A positive deflection will then appear. In our case this positive deflection has a duration of 0.04 second, a period of time generally considered normal for the travel of the impulse across the interventricular septum.

The only electroendocardiographic tracing published by Wilson and coworkers[37] of right bundle branch block in a dog does not show this initial positive deflection, a circumstance which the authors attribute to the initial positivity of the ventricular cavity not coinciding with the beginning of QRS group, as generally happens.

In the standard leads in cases of right bundle branch block, this initial phase of depolarization from left to right of the septum, which should produce a negative wave in Lead I, frequently does not appear because it is neutralized by the electromotive forces of depolarization of the thick wall of the left ventricle. Under these conditions the excitation of the septum can be traced only by placing the electrode close to it.

The left ventricular cavity remains negative during the entire QRS interval, as is shown by the endocardiac record (Fig. 17) published by Wilson and associates.[37] The excitation wave reaches the left ventricle first; the right ventricle receives the impulse after some delay. Due to the abnormal course of the excitation wave, potentials which at first move away from and later approach the right ventricle will result. This explains the peculiarities of the QRS complex observed in disorders of this type. Once the impulse has penetrated the septum and reached the fibers of the Purkinje system of the right ventricle, this chamber is rapidly depolarized from the subendocardial to the subepicardial area. During

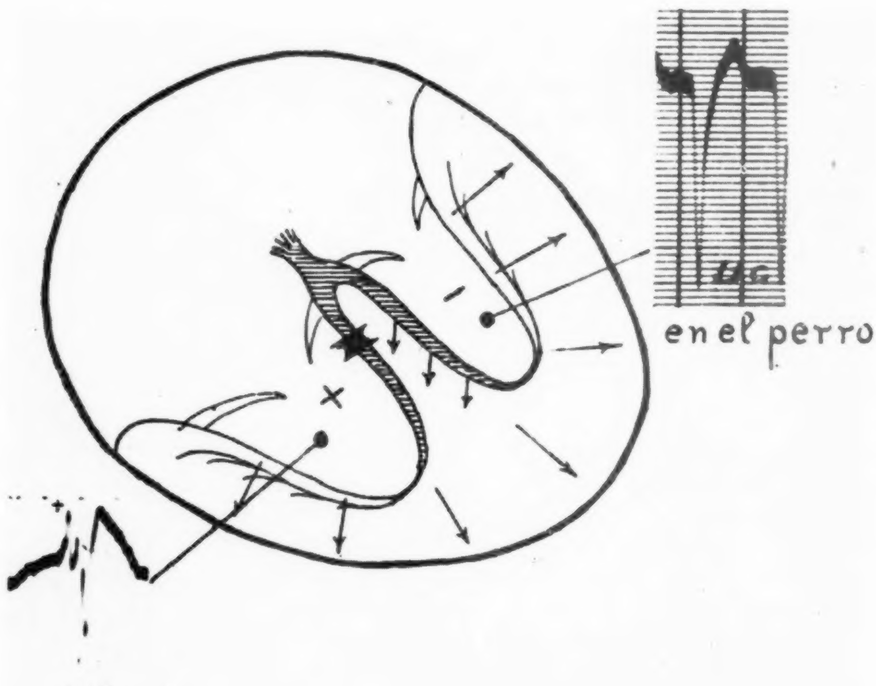


Fig. 17.—Variations of potential of the ventricular cavities in right bundle branch block. The endocardiac electrogram of the right ventricle is from a case of bundle branch block (in man). The electrogram shows the initial positivity of the right ventricle. The endocardiac electrogram of the left ventricle followed experimental bundle block in a dog (Wilson and associates). The ventricular cavity remains negative during all the period of inscription of the rapid ventricular complex.

this last phase, the right ventricular cavity remains negative, a condition evidenced in the electroendocardiogram by a negative deflection.

In left ventricular extrasystoles the developments are somewhat similar to those that occur in right bundle branch block. Because of the abnormal direction of the excitation wave, a positive potential develops in the right ventricular cavity, which we were able to trace in one such case (Fig. 18).

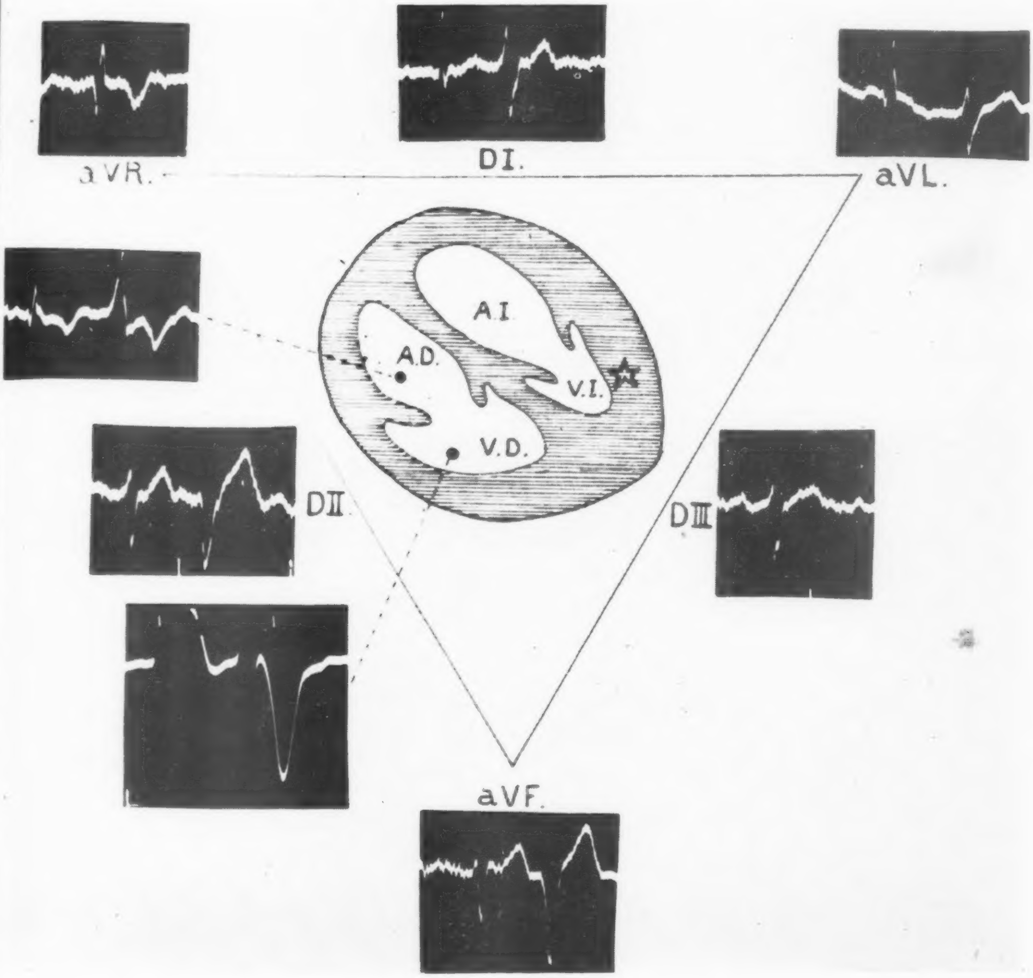


Fig. 18.—Endocardiac electrogram in a case of left ventricular extrasystoles. A record obtained with the electrode placed in the right ventricle and in the right auricle (see text).

ENDOCARDIAC ELECTROCARDIOGRAM IN A CASE OF AURICULAR EXTRASYSTOLES

In one of our cases, the endocardiac tracing made with the electrode placed in the right auricle (Fig. 19) showed a series of extrasystoles of auricular origin. In this tracing with a basic sinus rhythm, each ventricular complex is preceded by its corresponding auricular complex which comprises a positive wave followed by a negative deflection (normal *e*, *i*, *o* waves). When an auricular extrasystole occurs the positive wave disappears and only the negative deflection is present. A suitable explanation is that the extrasystole arises from a focus below the level of the electrode, or from some point relatively far from the electrode, so that the wave of depolarization moves away from it.

The auricular complex which precedes the premature contraction shows almost systematically an increase of voltage just before the extrasystole appears.

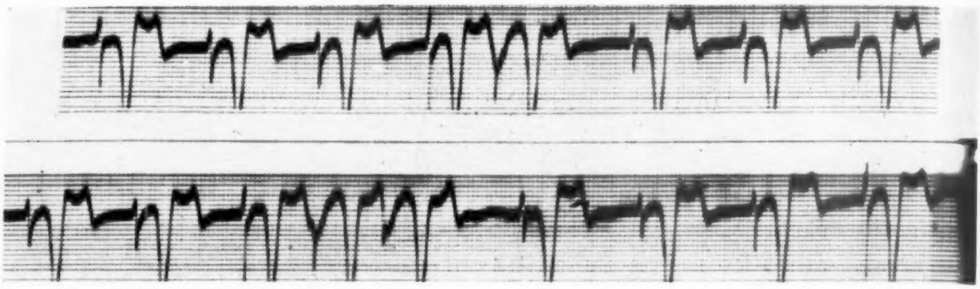
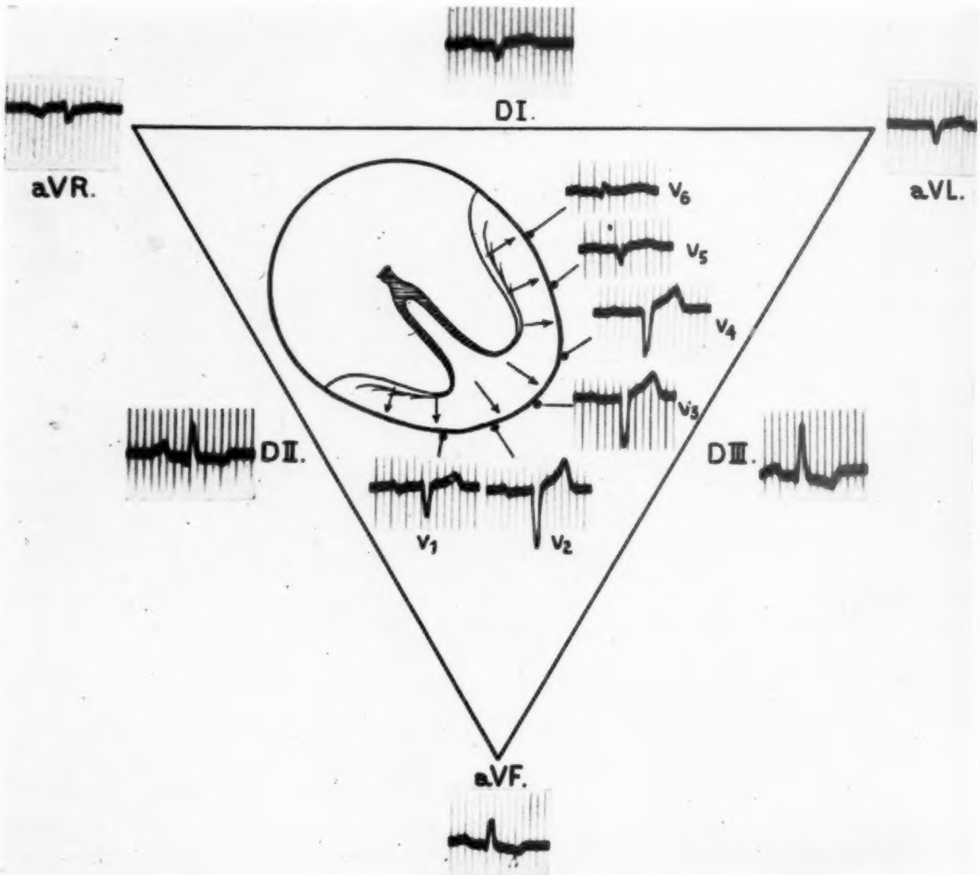


Fig. 19.—Endocardiac electrogram in a case of auricular extrasystoles. (Electrode placed in the right auricle.) The cardiac cycle preceding the extrasystole (Ex. A) shows an auricular complex (P wave) of much greater amplitude. The P wave of the extrasystolic contraction lacks of the positive potential shown by the normal P waves of the rest of the record. This indicates that the focus of origin of the extrasystole is situated in the lower portion of the auricle or below the active electrode.



A.

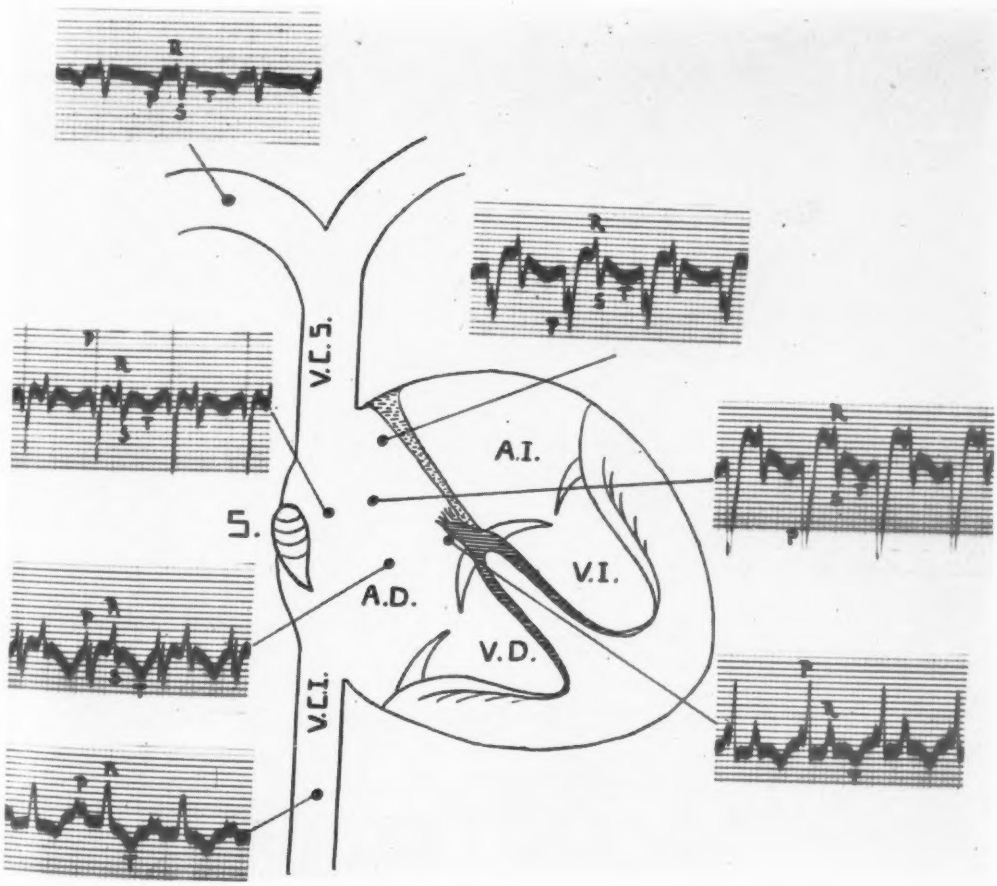
Fig. 20.—*A*, Electrocardiogram in standard leads, unipolar limb leads, and precordial leads in a case of myocardial infarct and deformation of P wave (notched P wave in Leads II and III). *B*, Endocardiac electrograms of the same case obtained at different levels of the auricular cavity. The notching of P can be observed in certain positions much more distinctly than in common leads (see text).

ENDOCARDIAC ELECTROCARDIOGRAM IN AURICULAR ASYNCHRONISM

Definite notching of the P wave in standard leads, especially in Lead I and Lead II, with other concomitant abnormalities, such as widening of the base, is regarded as evidence of pathologic alteration of the auricles.

The cause of notching of P has not been settled definitely. Some authors believe that it is due to an abnormal spread of the activation process through the auricles, that the electrical effect of the depolarization process undergone by each auricle is different. According to this theory the notch would simply indicate auricular asynchronism. Notching of the P wave may also indicate occasionally the existence of focal lesions in the auricular wall.

In one of our endocardiac electrograms made with the electrode in the right auricle (Fig. 20), a notched and broadened P wave appeared in Lead II and Lead



B.

Fig. 20 (Cont'd).—For complete legend see opposite page.

III. The shape of the auricular complex varied fundamentally according to the position of the electrode inside the auricle, but in almost all tracings the notching of P is clearly seen. During the depolarization period of the auricle, a downward double deflection is recorded if the electrode is placed in the upper portion of the auricle. With the electrode in a medial position, a W type complex is obtained. When the electrode is placed in the lower portion of the auricle, both deflections are directed upward. We interpret the first peak of P to be the result of activity of the right auricle and the second peak of activity of the left auricle.

The fact that no notching of P has appeared in our normal cases does not confirm Pardee's assumption[40] that the normal P wave is the algebraic summation of the electric effects produced in each auricle. Were this the case, the endocardiac electrocardiogram would record the activity of both auricles better than any of the ordinary methods.

We are therefore inclined to assume that in normal conditions the depolarizing wave originates in the node and spreads regularly over all the wall of both auricles, as if there were only one cavity. Notching of P is the expression of an alteration in the conduction of the impulse: either one of the auricles receives the impulse after some delay or the depolarization process is accomplished abnormally.

SUMMARY

The electrocardiographic variations registered by endocardiac catheterization in man are described on the basis of twenty-three cases studied.

The tracings show mainly the variations of potential of the heart, detected at the endocardiac surface. Endocardiac leads can be considered to be direct leads. The tracings are endocardiac electrograms.

The auricular endocardiac electrogram (endocardiac P wave) consists normally of a series of rapid deflections (S, *e*, *i*, *o* waves) joined to a final slow deflection (Ta wave) by means of the *o-u* segment. The shape of the auricular electroendogram undergoes modifications according to the position of the electrode inside the auricle.

Rapid deflections represent the process of depolarization of the auricles. Repolarization is represented by the final slow portion, as in the ventricular complex.

The initial negative deflection (S wave) of the auricular complex is regarded as an exponent of the activity of the sino-auricular node.

The endocardiac ventricular electrogram undergoes modifications in shape, depending upon whether the electrode is placed in the right ventricle or right auricle.

The electroendogram obtained from the ventricle (type I) shows an initial positive deviation (R wave) produced by the excitation of the interventricular septum which is followed by a negative deflection of large amplitude (S wave) and a large negative T wave. The waves of depolarization and of repolarization of the ventricular wall (R waves and T waves) have, then, the same direction.

The positive deviation of the S-T segment is greater as the catheter approaches nearer the septum.

The ventricular electroendogram recorded from inside the auricle (type II) traces the negative potentials of the ventricular activity during the spreading of the excitation wave. It begins with a negative deflection (Q or QS wave) followed by a positive deviation, an inconstant element, and ends in a T wave which is usually negative, sharply pointed, and deep. The ventricular complex of this type of tracing is similar to the ventricular complex of the esophageal electrocardiogram obtained when the catheter is at the level of the auricle.

The variations of endocardiac potential in bundle branch block, in one case of auricular extrasystoles, in one case of auricular asynchronism, and in cases of premature contractions of the right and left ventricles are described.

The electrocardiographic curves registered with the catheter placed in the superior and inferior venae cavae and at different sites in the venous system are described.

In bundle branch block of the common type, the endocardiac electrogram taken from inside the ventricle shows the absence of the initial positive (R) wave as a result of the abnormal excitation of the interventricular septum which is accomplished from right to left. The right ventricular cavity remains negative during the inscription of QRS complex. In bundle branch block of the uncommon type the right ventricular cavity is initially positive.

In the cases of bundle branch block which were studied the endocardiac electrogram shows the same characteristics that have been observed in experimental bundle branch block in the dog.

Since our paper was completed, a paper dealing with the same subject has been published by Hecht in the AMERICAN HEART JOURNAL **32:** 39, 1946. Hecht's conclusions do not coincide with our conclusions in all respects.

39

REFERENCES

1. Forssmann, W. I.: Die Sondierung des rechten Herzens, Klin. Wchnschr. **8:**2085, 1929.
2. Klein, O.: Zur Bestimmung des zirk latorischen Minutenvolumens beim Menschen nach den Fickschen Prinzip, Mün hen. m d. Wchnschr. **77:**1311, 1930.
3. Padilla, T., Cossio, P., and B consky, I.: Sondeo del corazón: Determinación del volumen minuto circulatorio, Semana méd. **2:**445, 1932.
4. McMichael, J., and Sharpey-Schafer, E. P.: Cardiac Output in Man by a Direct Fick Method, Brit. Heart J. **6:**33, 1944.
5. Cournand, A.: Measurement of the Cardiac Output in Man Using the Right Heart Catheterization, Federation Proc. **4:**207, 1945.
6. Cournand, A., and Ranges, H.: Catheterization of the Right Auricle in Man, Proc. Soc. Exper. Biol. & Med. **46:**462, 1941.
7. Stead, E. A., Jr., Warren, J. V., Merrill, A. J., and Brannon, E. S.: The Cardiac Output in Male Subjects as Measured by the Technique of Right Atrial Catheterization. Normal Values With Observations on the Effect of Anxiety and Tilting, J. Clin. Investigation **24:**326, 1945.
8. Richards, D. W.: The Circulation in Traumatic Shock in Man, Bull. New York Acad. Med. **20:**363, 1944.
9. Warren, J. V., Brannon, E. S., Stead, E. A., Jr., and Merrill, A. J.: The Effect of Venisection and the Pooling of Blood in Extremities on the Atrial Pressure and Cardiac Output in Normal Subjects With Observations on Acute Circulatory Collapse in Three Instances, J. Clin. Investigation **24:**337, 1945.
10. Brannon, E. S., Merrill, A. J., Warren, J. V., and Stead, E. A., Jr.: The Cardiac Output in Patients With Chronic Anemia as Measured by the Technique of Right Atrial Catheterization, J. Clin. Investigation **24:**332, 1945.
11. Brannon, E. S., Stead, E. A., Jr., Warren, J. V., and Merrill, A. J.: Hemodynamics of Acute Hemorrhage in Man, AM. HEART J. **31:**407, 1946.
12. Merrill, A. J., Warren, J. V., Stead, E. A., Jr., and Brannon, E. S.: The Circulation in Penetrating Wounds of the Chest: A Study by the Method of Right Heart Catheterization, AM. HEART J. **31:**413, 1946.

13. Warren, J. V., Brannon, E. S., Stead, E. A., Jr., and Merrill, A. J.: Pericardial Tamponade From Stab Wound of the Heart and Pericardial Effusion or Empyema; A Study Utilizing the Method of Right Heart Catheterization, AM. HEART J. **31**:418, 1946.
14. Richards, D. W.: Cardiac Output by the Catheterization Technique, in Various Clinical Conditions, Federation Proc. **4**:215, 1945.
15. McMichael, J., and Sharpey-Schafer, E. P.: The Action of Intravenous Digoxin in Man, Quart. J. Med. **13**:123, 1944.
16. Brannon, E. S., Weens, H. S., and Warren, J. V.: Atrial Septal Defect. Study of Hemodynamics by the Technique of Right Heart Catheterization. Am. J. M. Sc. **210**:480, 1945.
17. Moniz, E., de Carvalho, L., and Lima, A.: Angiopneumographie, Presse méd. **39**:996, 1931.
18. Padilla, T., Cassio, P., and Berconsky, I.: Sondeo de corazón. La vena cava superior y el borde derecho de la sombra de proyección de los grandes vasos de la base, Semana méd. **2**:391, 1932.
19. Ameuille, P., Ronneaux, G., Hinault, V., Desgrez, H., and Lemoine, J. M.: Remarques sur quelques cas d'artériographie pulmonaire chez l'homme vivant, Bull. et mém. Soc. méd. d. hôp. de Paris **60**:729, 1936.
20. Padilla, T., Cossio, P., and Berconsky, I.: Sondeo del corazón (Técnica), Semana méd. **2**:79, 1932.
21. Wolferth, C. C., Bellet, S., Livezey, M. M., and Murphy, F.: Negative Displacement of the RS-T Segment in the Electrocardiogram and Its Relationships to Positive Displacement; and Experimental Study, AM. HEART J. **29**:220, 1945.
22. Wilson, F. N., Macleod, A. G., and Barker, P. S.: The Order of Ventricular Excitation in Human Bundle-branch Block, AM. HEART J. **7**:305, 1932.
23. Macleod, A. G., and Cohn, A. E.: A New Piezoelectric Manometer to Record Intracardiac Pressures and for the Simultaneous Recording of Intracardiac Electrograms, AM. HEART J. **21**:345, 1941.
24. Wilson, F. N., Johnston, F. D., and Hill, I. G.: Interpretation of the Galvanometric Curves Obtained When One Electrode Is Distant From the Heart and the Other Near or in Contact With the Ventricular Surface, AM. HEART J. **10**:176, 1934.
25. Brown, W. H.: A Study of the Esophageal Lead in Clinical Electrocardiography, AM. HEART J. **12**:1, 307, 1936.
26. Wedd, A. M., and Stroud, W. D.: The Spread of the Excitation Wave Related to the Standard Electrocardiogram in the Dog's Heart, Heart **9**:15, 1921-1922.
27. Eyster, J. A. E., and Meek, W. J.: Interpretation of the Normal E.C.G. A Critical and Experimental Study, Arch. Int. Med. **11**:204, 1913.
28. Rijlant, P.: Courants d'action du coeur humain enregistrés à l'oscillographe cathodique, Gaz. Med. de France **4**:15, 1934.
29. Lewis, T., Meakins, J., and White, P. D.: The Excitatory Process in the Dog's Heart. Part I. The Auricles, Phil. Trans. Roy. Soc. *B*.CCV., 375, 1914 (cited by Brown, H. W.).
30. Hering, H. E.: Ueber die Finalschwankung (Ta Zacke) des Vorhofselektrogramms, Pflügers Arch. f. d. ges. Physiol. **144**:1, 1912.
31. Boden, E., and Neukirch, P.: Elektrokardiographische Studien am isolierten Säugetier und Menschenherzen bei direkter und indirekter Ableitung, Pflügers Arch. f. d. ges. Physiol. 146, 1918.
32. Sprague, H. B., and White, P. D.: Clinical Observations on the T Wave of the Auricle Appearing in the Human Electrocardiogram, J. Clin. Investigation **1**:389, 1925.
33. Lewis, T., and Rothschild, M. A.: The Excitatory Process in Dog's Heart. Part II. The Ventricles, Phil. Trans. Roy. Soc. *B*, *206*, 181, 1915.
34. Ashman, R., and Hull, E.: Essentials of Electrocardiography, ed. 2, New York, 1941, The Macmillan Company.
35. Pardee, H. E. B., and Goldenberg, M.: Electrocardiographic Features of Myocardial Infarction as Affected by Involvement of the Septum and by Complete and Incomplete Transmural Involvement, AM. HEART J. **30**:367, 1945.
36. Helm, J. D., Jr., Helm, G. H., and Wolferth, C. C.: The Distribution of the Potential of Ventricular Origin Below the Diaphragm and in the Esophagus, AM. HEART J. **27**:755, 1944.
37. Wilson, F. N., Johnston, F. D., Rosembaum, F. F., Erlanger, H., Kossmann, C. E., Hecht, H., Cotrim, N., Menezes de Oliveira, R., Scarsi, R., and Barker, P. S.: The Precordial Electrocardiogram, AM. HEART J. **27**:19, 1944.
38. Battro, A., Braun Menéndez, E., and Orías, O.: Asincronismo de la contracción ventricular en el bloqueo de rama, Rev. argent. de cardiol. **3**:325, 1937.
39. Glomset, D. J., Glomset, A. T. A., and Birge, R. F.: Morphologic Study of the Cardiac Conduction System. Part III. Bundle Branch Block, AM. HEART J. **28**:348, 1944.
40. Pardee, H. E. B.: Clinical Aspects of the Electrocardiogram, ed. 4, New York, 1941, Paul B. Hoeber, Inc.

MYOCARDIAL DEPRESSION IN SHOCK

A Survey of Cardiodynamic Studies

Carl J. Wiggers, M.D.
Cleveland, Ohio

APPROXIMATELY sixty years ago, a change in thinking began with respect to the cause of circulatory failure in shock. Previous to that time shock had been attributed to cardiac failure, and its treatment consisted in application of cardiac stimulants or, more precisely, drugs reputed to have such action. With the publication of Groenigen's monograph in 1885 and of Crile's treatise in 1890, the default of the circulation was assigned to the peripheral circulation. Following Henderson's demonstrations[1,2] that cardiac output and stroke volumes are reduced in shock as in hemorrhage,[3] and the more recent demonstrations that reduction in circulatory volume, venous return, and cardiac output precede the fall in arterial pressure,[4] it came to be accepted that reduction in cardiac output secondary to reduction in venous return was the initiating factor in shock. This constitutes the basic physiology upon which treatment by transfusions of blood, plasma, or substitutes is based. However, military, clinical, and laboratory experiences during World War II are in general agreement that such transfusions are of only temporary benefit in many cases of hemorrhage or shock. In other words, shock, as currently diagnosed, is either reversible or irreversible by adequate transfusions. The hope must not be abandoned that shock may prove to be reversible by other means; but pending such accomplishment we may differentiate between impending or reversible and irreversible states, particularly since evidence is accumulating that generalized cellular damage exists in the latter.

Important as these contributions have been, they do not explain the mechanisms of circulatory failure which redevelop in irreversible states after restoration of normal blood volumes by transfusion. Probably the most plausible and generally accepted hypothesis has been that cardiac output again decreases progressively because venous return fails again. This, however, only leads to another question as to the factors responsible for redevelopment and return of shock. At the beginning of World War II it was the dominant opinion that transfused fluids, including their colloids, continue to be lost from the circulation because capillary endothelium throughout the body becomes more permeable as a result of

From the Department of Physiology of the School of Medicine of Western Reserve University.
The investigations surveyed were supported by grants from the Commonwealth Fund.
Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

vasoconstriction, hypotension, anoxemia, or toxemia.[5] In reviewing the evidence in 1942, I[6] ventured to point out that this concept had been built on plausible assumptions rather than on substantial experimental evidence. As a result of additional studies on patients and animals recently reviewed by Gregersen,[7] this mechanism seems to have been discredited. In the most common forms of shock, reduction in blood volume occurs chiefly at the time of injury and the progressive circulatory failure which follows cannot be ascribed to a gradual decrease in blood volume. Obviously the default must lie in the cardiovascular apparatus.

During the past six years my associates and I have elected to study the hemodynamics of hemorrhage and shock with the hope of elucidating especially the cardiovascular mechanisms involved in irreversibility, an inquiry which even exceeds in importance the establishment of initiating factors. During these studies we have repeatedly published results which raised the question whether, in our zeal to implicate peripheral mechanisms, myocardial depression may have been overlooked as a factor or its importance minimized. Suspicions that the myocardium may be depressed in shock have been voiced by a number of other competent investigators, among them Howell,[8] Henderson,[9] and Erlanger and Gasser.[10] However, in view of immediately beneficial effects of infusions, they, as well as other authorities, did not regard the degree of myocardial depression of great importance. More recently other investigators[11-14] have laid greater stress on the existence and possible importance of myocardial damage, but the question whether cardiac filling and expulsion is really reduced at equivalent filling pressures has not been heretofore examined. This, in accordance with laws formulated by Henderson and Starling, would seem to be the supreme test.

This report attempts to summarize and integrate our evidence for the coexistence of myocardial depression in irreversible shock, obtained by different approaches to the problem.

METHODS

Standard Methods for Producing Hemorrhagic Shock.—Since the preponderance of evidence indicates that the most common forms of shock are initiated by reduction in effective circulating blood volume, the simplest and most controllable method for induction of shock should be by bleeding. However, at the inception of this work (1940) it had not proved possible to produce shock with certainty by bleeding; animals either died of cardiorespiratory failure or survived. As a result of many studies in other institutions as well as in our own, a number of standard procedures have been evolved to produce standardized hemorrhagic shock (for references, see Gregersen[7]). In general, these methods fall into two groups: (1) those employing withdrawal of a certain per cent of the estimated blood volume of animals and (2) those employing withdrawal of volumes sufficient to reduce arterial pressure to definite low levels. Many trials have shown that bleeding of animals on the basis of body weight is not practical because of many variables involved. Bleeding a certain percentage of the predetermined blood volume has proved more successful. Experience has shown that rather rapid bleeding until the blood volume is reduced to 40 to 48 per cent

of normal eventuates in hemorrhagic shock with fair consistency.[7] While absolute figures are still not available, our recent studies on inferior cava flow indicate that such reduction in blood volume reduces total venous return to approximately one-fourth to one-sixth of the normal. However, corresponding reductions in venous return can be produced by smaller decreases of blood volume if other factors, such as operations and anesthesia, themselves operate to reduce venous return. Therefore, extreme care and caution must be exercised to prevent supervention of such factors which affect venous return. This somewhat limits use of the procedures in the study of cardiovascular dynamics of standard hemorrhagic shock. In such investigations which require the use of anesthesia and variable operative procedures, our procedure, based on many preliminary trials by Werle and myself,[15] refined in association with Huizenga and Brofman,[16] and now used in over 400 dogs by various groups, has proved more suitable in our hands.

The method consists briefly of the following steps: (1) bleeding of a dog from a femoral artery at a rate of about 50 c.c. per minute until arterial mean pressure is reduced to 50 mm. Hg; (2) maintenance of this pressure for ninety minutes, if necessary by additional small withdrawals of blood during the early period; (3) further reduction of arterial mean pressure to 30 mm. Hg by careful additional bleeding; (4) maintenance of arterial pressure at this critical level for forty-five minutes, giving small intravenous infusions toward the end of this period if necessary; (5) intravenous reinfusion of all blood withdrawn into heparin after filtration and warming, at a rate less than 50 c.c. per minute (this generally results in reasonable recovery of arterial pressure for periods of one-half to one hour); (6) observation of the development of shock which causes arterial pressures to fall progressively to 40 mm. Hg or less in three to six hours. These changes in mean arterial pressure are indicated in Fig. 2. This standard procedure not only serves to produce irreversible hemorrhagic shock, which has a fairly standard hemodynamic course in different dogs, but also *enables us to compare in the same animal the hemodynamic changes produced during states of hypovolemia (posthemorrhagic hypotension) with those that develop spontaneously during states of normovolemia (postinfusion failure)*. Comparison with controls in the same animals[16] have shown that the average reduction in blood volume after postinfusion circulatory failure amounts to only 0.7 ±1.64 c.c. per kilogram.

Anesthesia and Operative Procedures.—It is a primary requisite in experimental studies of shock that the condition produced shall be reasonably identical with that observed in various forms of shock in man. In 1942 I[6] presented arguments that this can be accomplished best when dogs are properly anesthetized with morphine and barbital. In the six years during which this anesthetic was used, our belief has been corroborated that experiments so performed are better standardized and permit more secure deductions than those performed under local or temporary ether anesthesia. An hour or two after induction of morphine-barbital anesthesia, arterial and central venous pressures as well as cardiac output are fully equal to those reported by others on unanesthetized dogs.[17] However, the use of continuous general anesthetics is still deplored by some investigators.

Gregresen[7] has recently restated the following drawbacks to the use of anesthetized animals: (1) Since it is impossible to reproduce all clinical signs of shock during a state of anesthesia, it is difficult to be certain that comparable conditions have been produced. (2) This is possible by use of temporary ether anesthesia or, in certain types of experiments, local anesthesia. (3) Permanent anesthesia modifies compensatory reactions so that bodily changes differ quantitatively and qualitatively from those of the normal body. To these the following may be added: According to several reports,[18,19] administration of morphine or barbital after hemorrhage or during impending shock intensifies the circulatory failure.

To these objections the following answers can be made categorically: (1) Unfortunately certain clinical signs, for example, sweating and pallor, are not observable in dogs, anesthetized or unanesthetized. Muscular tension and activity vary considerably in clinical cases of shock, and the characteristic facial expressions and general appearance of patients in shock also occur in other acute clinical states which do not eventuate in shock. The cardinal signs, reduction in cardiac output, arterial pressure, and peripheral blood flow, occur in barbitalized dogs as in clinical shock even after large transfusions. It is true that cardiac acceleration precedes initial changes of shock in barbitalized animals, but it is also true that few patients suffer injury or wounds without a preceding acceleration of their hearts due to psychic reactions or muscular effort. Finally, if anesthesia obscures signs of shock, it should likewise be difficult to recognize its occurrence in patients in the operating room—a view to which surgeons are not likely to subscribe. (2) Use of temporary ether anesthesia during infliction of injury or bleeding affects compensatory reflex responses more than does barbiturate anesthesia. It induces excessive hyperventilation and was probably responsible for low CO_2 content and pCO_2 of blood reported by the Columbia investigators.[7] While local anesthesia or nerve block are unquestionably useful in the study of many shock problems, cerebral reactions develop in dogs during bleeding which cause whining, restlessness, struggling, irregular breathing, exacerbations of arterial pressure. These make it difficult or impossible to evaluate dynamic changes in the heart or circulation per se. (3) No experimental evidence exists for the statement that qualitative or quantitative differences occur in compensatory reactions during shock produced in unanesthetized and properly barbitalized dogs. As far as known, all the cardiovascular and respiratory reflexes evoked from somatic and visceral structures are present during morphine-barbital anesthesia. It has perhaps not been sufficiently emphasized that the changes in temperature regulation and blood concentration reported by Green and associates[20] from our laboratory are consequences of light barbiturate anesthesia, which is known to cause shivering or clonic muscular movements. It is true that the spleen is enormously engorged and, on excision, may yield 150 to 200 c.c. of blood in a dog weighing 10 kilograms, but it empties rather completely within fifteen minutes after a large hemorrhage and remains constricted throughout experiments such as ours.[21] (4) Unquestionably any anesthetic, including morphine and barbital, administered *after* severe hemorrhage, exerts deleterious effects. However, given one and one-half to two hours previous

to experimental procedures, it renders dogs and guinea pigs more resistant to blood loss and posthemorrhagic hypotension.[22,23]

While we feel satisfied that anesthesia introduces no serious problem, there can be no question that coincident operative procedures hasten and accentuate the development of shock. Our studies on the heart and circulation were therefore carried out as far as possible on animals submitted to very minor operative procedures. However, it proved necessary to extend these with experiments requiring exposure of the heart. In applying instrumentation primarily evolved to study acute reactions of the myocardium to experiments which extend over many hours and which, in addition, require artificial respiration and opening of the chest, it was necessary to evaluate the extent to which surgical "shock factors" complicate those due to hemorrhagic hypotension. Despite the fact that every known expedient was used to reduce such contributing factors, approximately half of such animals tolerated less loss of blood, withstood periods of 50 and 30 mm. Hg hypotension for shorter intervals, and developed post-infusion circulatory failure more rapidly. Fortunately, it was found that, if accidental occult hemorrhage after reinfusion of heparinized blood is avoided, comparable sequential dynamic states occur in operated and essentially unoperated dogs, the only difference being the speed with which reactions develop. However, when extensive operative procedures were required, we based our conclusions regarding myocardial impairment on those experiments in which the time courses, as well as arterial pulse patterns, most nearly corresponded with those of intact animals, rather than on statistical evaluation of all experiments, including those in which uncontrollable variables entered.

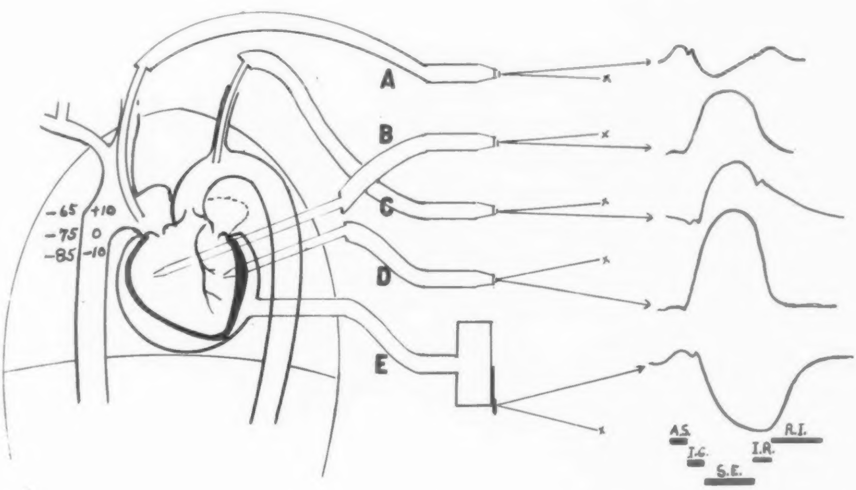


Fig. 1.—Scheme showing registration of dynamic changes of heart and representative curves under normal conditions. *A*, Pressure pulses of right atrium; *B*, same from right ventricle; *C*, same from aorta; *D*, same from left ventricle; *E*, volume curves of both ventricles. Records aligned at right with regard to phases of a heart cycle. *A.S.*, atrial systole; *I.C.*, isometric contraction; *S.E.*, systolic ejection; *I.R.*, isometric relaxation; *R.I.*, rapid inflow. Numerals on right indicate how effective venous pressure remains at 75 mm. water under different intrathoracic pressures.

EVALUATION OF CARDIODYNAMIC CHANGES

Methods for Evaluating Cardiodynamic Changes.—While a number of special techniques were used for special studies, the standard experiments involved various combinations of recordings diagrammatized in Fig. 1. They included registration by calibrated optical manometers of adequate frequency of pressure pulses in the right atrium, *A*, right ventricle, *B*, aortic arch, *C*, and left ventricle, *D*. By placing a cardiometer around the ventricles, phasic volume changes were recorded by calibrated systems, *E*. The types of curves recorded by each of these recorders are also illustrated in Fig. 1 with correct temporal and ordinate relations. With an understanding of their meaning, as analyzed in most textbooks of physiology, and a knowledge of changes induced by known variables, such a chart of curves serves the physiologist much as a master score does the conductor of an orchestra.

Aortic Pressure Pulses.—These are useful (1) in determining systolic and diastolic pressures exactly, (2) in calculation of changes in duration of ventricular systole with respect to diastole (or heart rate), and (3) in evaluating altered mechanisms of cardiac ejection at different states of arterial tension by changes in their configuration.

The sequential changes which occur in amplitude, contour, and time relations of curves during the course of the standard experiments outlined previously have been established and repeatedly confirmed. They are illustrated in Fig. 2 with reference to mean arterial pressure changes. Beat 1 is a control. Reduction of mean arterial pressure to 50 mm. Hg, *A*, within ten minutes or less reduces systolic more than diastolic pressure and thereby decreases the pulse pressure. The pulse pattern (Beat 2) is characterized by abridgement of the period of systolic ejection, development of a primary spike which is followed by a peaked summit, and this by a deep incisura. Following this, the pressure gradient declines more gradually than in control pulses. As more blood is withdrawn to maintain a constant hypotensive level, *A-B*, the pulse pressure decreases somewhat more, and curves are characterized by a slower rise, simple rounded contour, and a flat diastolic pressure as shown in Beat 3. These changes merely become intensified during the 30 mm. period, *B-C*, as shown by Beat 4.

Upon completion of the reinfusion of all withdrawn blood, mean pressure is restored to levels which may be somewhat below or somewhat above control levels in different animals; but the pressure soon levels off, as indicated in Fig. 1, *D-E*, at a plateau level 85 to 90 per cent of control mean pressure. Immediately after infusion, normal patterns of arterial pulses are restored (Beat 5). However, during the plateau level of mean pressure, the arterial pressure pulses usually display some reversion to a form which suggests deterioration of cardiac action. This constitutes the first phase of circulatory failure. The changes (Beat 6) include redevelopment of a primary spike, a more peaked systolic summit, an abridged ejection phase, a deep incisura, and a lower postincisural pressure. Apparently, mean pressure is maintained through progressive cardiac acceleration and compensatory vascular mechanisms despite some decrease in cardiac output.

A second stage of circulatory failure begins from one-half to one and one-half hours after reinfusion, *E*, and is signaled by a progressive decline of mean pressure to about 70 per cent of control values. Toward the end of the period, *E-F*, pulse pressure has been reduced, and the pulse patterns (Beat 7) revert to the simple form observed after bleeding (see Beat 5). As systolic, diastolic, and pulse pressures slowly decrease thereafter, this deterioration in form is accentuated, as shown in Beats 8 and 9. It is apparent that the changes in central pulse patterns which follow abstraction of blood from the circulatory system and those which develop spontaneously after its replacement do not differ essentially. However, it may be noted in Fig. 2 that after reinfusion the stepwise deterioration in form occurs at somewhat higher diastolic pressure levels than after bleeding.

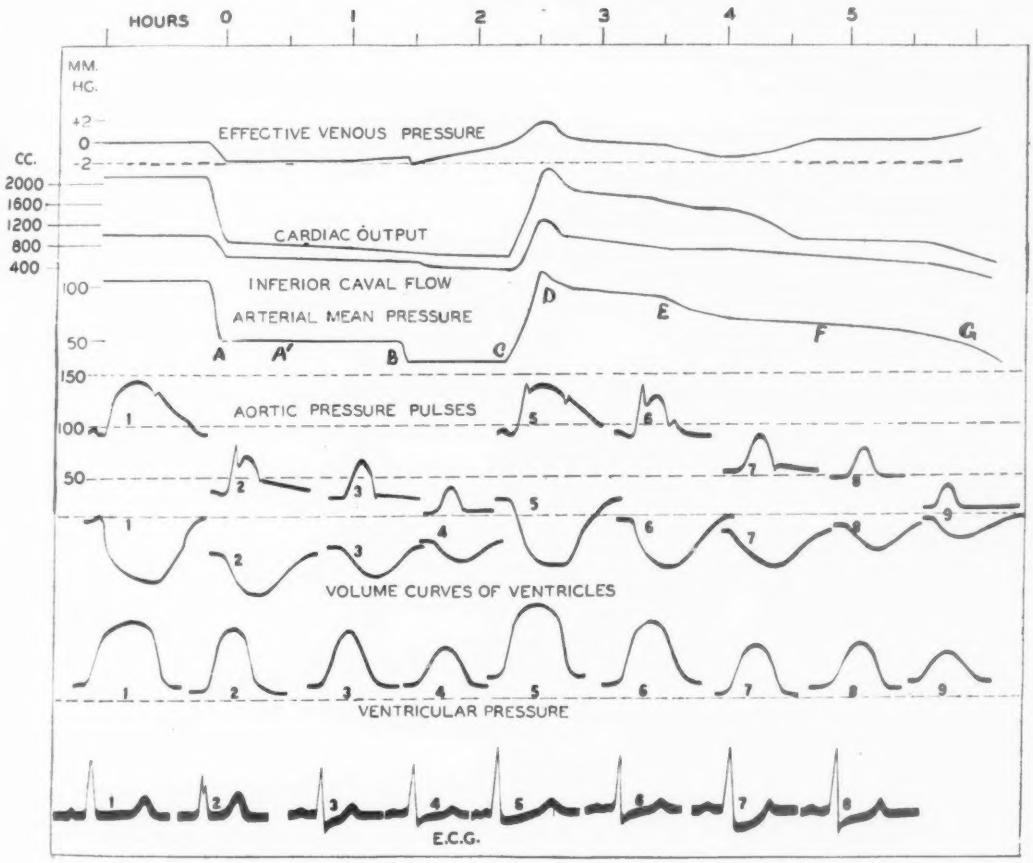


Fig. 2.—Chart interrelating cardiodynamic changes during hemorrhagic hypotension, reinfusion, and subsequent circulatory failure. Discussion in text.

Sequential Changes in Cardiac Output.—While it had been satisfactorily established that cardiac output decreases progressively both after hemorrhage and in various types of experimental shock,[1-3,25,26] it remained to be demonstrated that postinfusion circulatory failure of our experiments was also accompanied

by such changes. In order to obviate difficulties inherent in application of the Fick principle to dogs[27] and to realize more frequent determinations of cardiac output than that method allows, H. C. Wiggers[17] succeeded in eliminating certain faults in the Stewart method and in applying it to cardiac output determinations in intact dogs. Later, with Middleton,[28] the sequential changes in our standard experiments were established. The trend of these changes is indicated in Fig. 2. H. C. Wiggers and Middleton concluded that withdrawal of blood sufficient to reduce mean arterial pressure to 50 mm. Hg, *A*, promptly reduced cardiac output to 29 to 45 per cent of control values. Calculated stroke volume was more severely reduced during the latter part of this period because of the mechanical effect of cardiac acceleration. Only minor fluctuations occurred during the 30 mm. period, *B-C*. Following reinfusion of blood, *C-D*, cardiac output returned to or slightly exceeded control values in approximately one-half of the animals; it was restored to only 45 to 85 per cent of control values in the other half. Despite the fact that the circulating blood volume was almost equal to that at the start of the experiment,[16] progressive reduction of cardiac output gradually supervened even while mean arterial pressure was maintained, *D-E*. Continuing reduction in cardiac output appeared to be responsible for the decline of arterial pressure to 65 to 80 per cent (average 70 per cent) of control figures, *E-F*. Thereafter cardiac output tended to stabilize, and further decline of mean arterial pressure to 30 per cent of control figures, *F-G*, was apparently due to reduction in total peripheral resistance. These results demonstrated that postinfusion circulatory failure, like experimental and clinical types of shock, is associated with progressive reduction in cardiac output. However, reduction in blood volume is not necessary to produce these typical changes.

Central Venous Pressures.—Since the extent of ventricular filling and the volume of cardiac output are primarily determined by the venous filling pressure, it might be anticipated that the central venous or atrial pressure would undergo a decline if reduction in cardiac output during hemorrhagic shock were due to decreased venous return alone. Since the heart and large intrathoracic veins are under subatmospheric pressure, the atrial pressure available for right ventricular filling is not measured by pressure recorders balanced against atmospheric pressure; it must be calculated as the algebraic difference between such pressure and intrathoracic negative pressure measured at the same time; that is, by the effective venous pressure. Thus, as illustrated in Fig. 1, an effective venous pressure of say 75 mm. saline could be created with highly variable intra-atrial pressures. The estimation of effective venous pressure is especially important in these studies, for, as found in our early studies,[16,29] intrathoracic pressure changes significantly during bleeding and reinfusion. We also realized early that exact measurement of central venous pressure and calculation of effective venous pressure is not the simple procedure that it is generally believed to be. Considered judgment as to points of measurement, in addition to fidelity in registration, is important. In our first studies[29] we measured venous pressure of optical pressure records just before ventricular systole (*Z* on atrial curve of Fig. 3) and determined intrathoracic mediastinal pressure *at the same moment during expiratory*

rest. It was found after bleeding that recorded and effective venous pressures both decreased definitely but not proportionately; both tended to rise slightly during the period of drastic hemorrhagic hypotension (Fig. 2, *B-C*). During the postinfusional failure, decline of arterial pressures (Fig. 2, *E-G*) and deterioration of pressure pulses occurred *without decrease in effective venous pressure below control levels* in eight of twelve experiments. This suggested that any tendency for venous return to decrease may be nicely counterbalanced by decrease in cardiac output, which, if true, suggests primary myocardial depression.

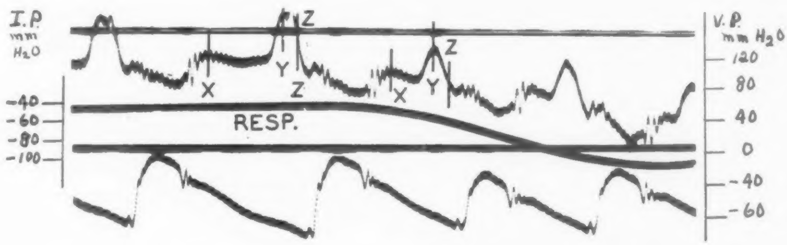


Fig. 3.—Pressure pulses from right atrium (upper curve) and aorta (lower curve) of a normal dog, related to intrathoracic pressure changes recorded by a calibrated air manometer. Inspiration, downward movement. Upper curves show the considerable phasic variations which exist during cardiac cycles and the still greater variations due to respiration. The importance of selecting fixed points or obtaining average pressure during expiratory rest is evident.

The changes in effective venous pressure were again studied in thirty-five dogs after our procedure for producing hemorrhagic shock had been better perfected.[16] In this research, *average venous pressures during an expiratory phase* were used in calculations of effective venous pressure. The experiments in which postinfusion circulatory failure was accompanied by reduced and essentially normal effective venous pressures were divided appioximately equally. It appeared obvious that the decline of arterial pressure, reduction of cardiac output, and deterioration of arterial pressure pulses after transfusion is sometimes, but not necessarily, accompanied by a decline of recorded and effective venous pressures.

Establishment of the trend of effective venous pressures seemed so important that measurements of intrathoracic and venous pressures were continued in forty-eight more experiments in which other circulatory phenomena were under investigation. Comparisons between control effective venous pressures and those which developed at different comparable periods of experiments were made.[30] It suffices for present purposes to recall that when arterial pressure had again declined to 50 mm. after reinfusion, effective venous pressures were below control values in eighteen dogs only; they were near or above control values in thirty dogs. Indeed, the lowest effective venous pressure of the latter group was 60 mm. saline, a value commonly regarded as normal for dogs.

While the principle for determining effective venous pressures is sound, the possibility exists that technical errors can be introduced in determination of intrathoracic pressure; for example, by development of air pockets of varying

size in the pleural cavity or in other regions of the thorax. To check this contingency, twelve supplementary experiments were performed[30] on dogs with an effective pneumothorax under mild artificial respiration. Under these conditions the central venous pressure actually recorded represents the effective filling pressure. The results showed a decrease in right atrial pressure in nine and approximately normal pressure levels in only three aninals. For reasons analyzed at the time, the latter three were regarded as experiments which most nearly represented conditions in unoperated dogs, but this need not be stressed at the present time. If we add the experiments just reviewed, we find that during postinfusion shock effective venous pressure decreased in forty-eight animals and was essentially at normal levels in fifty-nine. This dominant trend is indicated in Fig. 1. Of special interest are the decline of effective venous pressure during *A-B*, the tendency to return toward normal during *B-C*, the supernormal elevation at *D*, the stabilization during *D-E*, the decline during *E-F*, and the ultimate rise during *F-G*. The fact that the progressive circulatory failure following transfusion occurred in so large a per cent of animals without significant reduction in effective venous pressure strongly suggested that myocardial depression supervened in the majority of our animals submitted only to minor operative procedure. It was important, however, to substantiate such deductions by more direct evidence and to elucidate the cardiac mechanism by which reduction in output is brought about in postinfusion shock.

Cardiometer Experiments.—Werle and I[31] studied the alterations in diastolic size, filling, and discharge of the ventricles by means of cardiometers during the course of similar hemorrhage experiments. Typical volume curves recorded optically at different times showed that stroke volumes and minute volumes were decreased consistently during both the periods of hemorrhagic hypotension and of shock following infusion, but the manner in which such reductions occurred in the latter period differed. In one group of animals (approximately half), reduction in stroke volume was accompanied by decrease in atrial pressure, reduced rate of ventricular filling, and decreased diastolic size at comparable heart rates. These resembled the effects produced by simple bleeding. In the other 50 per cent of experiments illustrated by volume curves in Fig. 2, atrial pressures during postinfusion failure were above control values and the diastolic size of the ventricles was greater, but the ventricular filling rate was still retarded. In these experiments it was also observed that diastolic size became greater during the period of 30 mm. Hg hypotension, while systolic discharge diminished (Fig. 2, volume curves *2*, *3*, and *4*). Since myocardial depression apparently occurred in this half of the experiments, the question arose as to whether existence of a similar myocardial depression might be masked in the other group of experiments in which central venous pressures decreased. It should be added parenthetically that since diastolic size is also a function of duration of diastolic filling (that is, heart rate), all of these conclusions are actually based on reconstruction of volume curves for identical heart rates. This cannot be depicted in the diagrams without disturbance of the correct time relations to other curves.

Investigators have been accustomed to infer that the myocardium is unaffected in shock because of repeated demonstrations that cardiac output can be restored by transfusions. However, it had not been demonstrated, as required by Starling's law, that such restoration of cardiac output occurs at normal venous pressures. That this is not true after prolonged hypotension was shown in two ways in our experiments: (1) Normal cardiac output or stroke volumes at equivalent heart rates after reinfusion occur only while venous pressures are far above control values; it is less when these return to control values (Fig. 2, volume curves *5* and *6*). (2) When small rapid transfusions were given just previous to final infusion at *C*, or when added transfusions were given during final circulatory failure, *E-G*, they restored control venous pressures temporarily, but systolic discharge remained below that during initial controls.

In order to study this response under more controllable venous pressures, Wegria, Guevara Rojas, and I[32] devised a heart-lung dog preparation. Among other observations it was established that a period of 50 mm. hypotension lasting for one to one and one-half hours decreases the ability of the ventricles to respond to equivalent venous pressures.

Ventricular Pressure Curves.—Opdyke and I[33] studied the changes in right ventricular pressures of intact animals and later compared changes in right and left ventricular pressures in exposed hearts during the course of hemorrhagic hypotension and shock. In records so obtained, conclusive evidence that myocardial depression occurs would be furnished if, either during the irreversible period of hemorrhagic hypotension or during postinfusion failure, initial tension increased while systolic ventricular pressure and systolic discharge decreased. This occurred in right ventricular pressure curves recorded from intact animals during later periods of prolonged hypotension as well as during postinfusion failure. Since the changes in initial tension correlated with alterations in effective venous pressure in the greatest number of animals, a few of these curves are reproduced in Fig. 2. However, since such changes might have resulted from uncontrollable variations of intrathoracic pressure or shifts in hydrostatic levels of the right ventricle, they cannot be regarded as quite conclusive. For this reason, further experiments were conducted on exposed hearts in which environmental pressure and hydrostatic positions of the ventricles could be kept constant. Unfortunately, it was not possible to record two curves on 12 cm. paper with sufficient amplitude, so that we could not always be certain of the existence of small differences in initial tension. However, records from five good experiments were meticulously measured and rechecked and an average curve constructed. This average curve showed clearly that initial tensions decrease in both ventricles after simple hemorrhage, but that initial tensions remain approximately at control levels during postinfusion failure when cardiac output has presumably decreased to an equivalent extent, as after bleeding. However, in an experiment considered to be our best, initial tensions declined during this period, just as after simple hemorrhage.

While these studies failed to settle the question as to whether the decreased ventricular force and discharge during postinfusion failure is associated with

unchanged or elevated initial tension, the changes in contour of the curves contributed to our understanding of the altered cardiodynamics. The alterations will be considered later.

Blood Flow in the Inferior Vena Cava.—Eckstein and associates,[34] in a series of thirteen experiments, recorded inferior cava flow by a differential pressure type of flowmeter. The trends of flow changes charted in Fig. 2 follow alterations in cardiac output determined in intact dogs in a general way. A similar correspondence in trends occurred between inferior cava flow and central venous pressure. Two exceptions must, however, be noted: (1) There appeared to be a lag in the elevation of central venous pressures and only a minor increase in cava flow until about one-fifth to one-fourth of the total blood withdrawn had been reinfused into the femoral vein. (2) During the late period of posthemorrhagic hypotension, *B-C*, and the second stage of postinfusion failure, *F-G*, inferior cava flow continued to decrease, but central venous pressures tended to stabilize or rose slowly toward normal levels. Inferior cava flow was consistently related to venous pressure gradients between the lower region of the inferior cava and right atrium but not necessarily to central venous pressure.

Electrocardiograms.—If, as appears probable from cardiodynamic studies, impairment of the myocardium is a factor in the unfavorable response to blood transfusion, it is reasonable to expect that a methodical series of electrocardiograms might reveal some changes. Manrique Izquieta and Pasternack[25] studied the configuration of electrocardiograms obtained by three standard leads and six chest leads paired with a central terminal. Displacement of the S-T segment in several leads, particularly in V_2 and V_3, and less often in Leads II and III, occurred during the late periods of hypotension (Fig. 2, electrocardiogram complexes 3 and 4). The electrocardiogram usually became normal again after infusion, but before arterial pressure had declined significantly, S-T displacement reappeared and the T waves often became larger and peaked (Fig. 2, electrocardiogram complexes 6, 7, and 8).

ANALYSIS OF RESULTS

In the previous section the experimental work was briefly reviewed, from which the underlying data assembled in Fig. 2 were derived. In the event of experimental discrepancies, reasons were given for the choice of exhibits. We shall now proceed to a vertical analysis of various periods of our experiments and attempt to formulate conceptions of the cardiodynamic mechanisms concerned.

Effects of Simple Hemorrhage.—The cardiodynamic effects produced by simple severe hemorrhage are exhibited during the first twenty or thirty minutes of the 50 mm. hypotension period, *A-A'*. All the changes which occur during this interval are usually reversible by reinfusion of substantial volumes of blood, plasma, or blood substitutes. In many cases isotonic saline infusion suffices to produce survival.

The low systolic and diastolic pressures and small pulse pressure (see Beats 1 and 2) are due to decreased systolic discharge and reduced minute output. This reduction, in turn, is secondary to decreased venous return. Inferior vena cava flow diminishes to 45 per cent of normal or less, actual and effective central venous pressures fall significantly, initial tension in the ventricles is decreased, and their diastolic size is less (see Beats 1 and 2). The changes in configuration of central pressure pulses already described are due to alterations in the mechanism of left ventricular ejection. Ventricular volume and pressure curves clearly show that duration of systole is less and that the ventricles expel their diminished contents in a shorter time, but still with good velocity and force. This sudden ejection into a lax aorta produces the characteristic overshoot of arterial pressure (Beat 2). However, the greatly diminished stroke volume is insufficient to maintain aortic pressure even during systole; pressure falls considerably toward the end of systole, the incisura after completion of systole is deep, and the diastolic portion is low. Electrocardiograms taken during this period reveal no changes which cannot be attributed to physical changes in the size and position of the heart after bleeding.

Effects of Oligemic Shock.—The succeeding 105 to 115 minutes of hypotension, *A′-C*, represent a period during which irreversible changes are produced. The cardiodynamic alterations are characteristic of progressive and terminal stages of shock associated with low blood volumes; that is, ***oligemic shock.*** If untreated, animals die of cardiorespiratory failure; if substantial transfusions are given, complete immediate recovery apparently occurs, but this is temporary and usually followed by slow progressive decline of arterial pressure and death. Previous to infusion, systolic and diastolic pressures do not change materially until further bleeding to 30 mm. Hg levels, *B-C*; occasionally systolic, diastolic, and pulse pressures decrease spontaneously without additional bleeding.

Reduced venous return indicated by further diminution of inferior cava flow could account for the further reduction of cardiac output and pulse pressure which obviously occurs during this stage of hypotension. However, examination of other occurrences indicates that cardiodynamic mechanisms are otherwise affected. Effective venous pressure, initial ventricular tension, and diastolic ventricular size all tend to return toward normal during the interval *B-C* instead of decreasing, as may be anticipated from effects of diminished inferior cava flow. Comparison of Beats 3 and 4 with Beat 2 shows that ventricular pressure curves rise more slowly, denoting that the force of contraction is decreasing; volume curves not only exhibit some increase in diastolic size and reduced strokes, but also a slower velocity of ejection. This lazy ventricular action accounts for the slower rise and rounded form of arterial pulse patterns in Beats 3 and 4. The systolic discharge is not sufficient to sustain diastolic pressure which remains at a low flat level. Such pressure pulses are diagnostic of stroke volumes barely sufficient to maintain any circulation. The deduction that myocardial depression has supervened is confirmed by appearance of S-T segment depression in electrocardiograms and by the fact that such hearts do not respond with normal stroke volumes when atrial pressure is temporarily raised to normal levels.

Immediate Effects of Infusion.—Immediately after reinfusion of all withdrawn blood at a rate of about 50 c.c. per minute, *C-D*, a large pressure difference exists between the inferior vena cava and the right atrium. The abdominal veins become a reservoir from which increased volumes of blood are delivered to the heart for five to fifteen minutes after infusion. Restoration of arterial pressures and forms of pressure pulses to normal are the most obvious effects. Intraventricular pressures of normal amplitude, contour, and duration redevelop; as a rule, the electrocardiogram again becomes normal. In the most successful experiments, cardiac output also returns to control values. However, all data show that, in order to produce these effects, the ventricles are required to operate under supernormal venous pressures and initial pressures compared with controls (see Beats 1 and 5). Inferior cava flow is increased over normal, effective venous pressure and initial tension are much elevated, and the diastolic ventricular size is tremendously increased. However, the stroke volume at equivalent heart rates is not greater than in control states. The ventricles are maintaining normal systolic discharges and output only because they are overstretched, a condition characteristic of incipient myocardial failure.

Normovolemic Postinfusion Shock.—The circulatory failure which develops after reinfusion usually occurs in three fairly distinct stages: *D-E, E-F, F-G.* The cardiovascular changes which develop during these stages characterize a type of shock which develops without significant reduction in blood volume; they are due solely to irreparable damage to the peripheral vessels, the heart, or both. It may, therefore, be designated *normovolemic shock.* The sequential hemodynamic changes deserve careful study, because they may have application to clinical forms of shock in which significient oligemia does not appear to exist, or in which shock develops despite restoration of a normal blood volume by transfusions.

Within fifteen minutes after reinfusion, inferior cava flow has returned to normal levels, but central venous pressures and initial tension in the ventricles still remain above control values. During the next ten or fifteen minutes cava flow and cardiac output are decreased materially. Comparison of Beats 5 and 6 reveals that the diastolic ventricular size is normal but the stroke volume is less. Ventricular pressure curves start with normal initial tensions and assume a rounded contour; the maximum intraventricular pressure is reduced, and systole is shortened. In short, the changes in cardiac behavior observed after simple hemorrhage with much greater reduction in venous return and with a marked decline of central venous and initial ventricular pressures now develop when these are essentially at normal levels. Electrocardiograms taken at this time reveal the reappearance of S-T segment depression. Despite this obvious depression of myocardial function, mean arterial pressure is maintained rather well, presumably through cardiac acceleration and continued viability of compensatory vascular mechanisms. However, arterial pressure pulses already mirror changes in the cardiac mechanism by changes in contour. These include redevelopment of a primary spike, a peaked summit in the abridged ejection phase, a deep incisura, and a lower postincisural pressure.

A second stage begins from one-half to one and one-half hours after reinfusion, *E-F*. It is signaled by a progressive decline of mean pressure to about 70 mm. and is due to progressive reduction in cardiac output. Inferior cava flow, effective venous pressure, initial pressures, and diastolic ventricular size all progressively decrease below control levels. Comparison of Beat 7 with Beat 6 shows the stroke volume is less and the velocity of ejection slower. Ventricular pressure curves display a slower rise and a lower maximum, indicating reduced force of contraction, and S-T segments of electrocardiograms continue to show displacement. Since all of these changes occur with reduction in venous return and effective venous pressure, any existing myocardial depression would tend to be obscured by concurrent reduction of venous return. However, *if normal venous flow and pressure are restored at this time by additional reinfusions, the stroke volume and cardiac output still remain below control values.*

A third stage is inaugurated about thirty minutes later by a further decline of arterial pressure and further deterioration of arterial pressure pulses, *F-G*. Since venous and initial pressures tend to rise while cardiac output becomes fairly stabilized, and the calculated total peripheral resistance is reduced, this decline appears to be chiefly of peripheral origin. The ventricles maintain their constant reduced output and force of contraction for a while by virtue of increasing diastolic stretch and initial tension. Ultimate failure of the heart comes about through development of deceleration and fairly great slowing. This reduces the cardiac output and arterial pressures very rapidly to low levels. When these are not sufficient to maintain activity of the respiratory center, death supervenes.

DISCUSSION

In the type of experiment outlined at the start, a protracted period of posthemorrhagic hypotension produces irreversible changes which affect the myocardium as well as other organs. As a result of such myocardial depression, reinfusion of all withdrawn blood restores cardiac output, arterial pressures, and contours of pressure pulses only because venous return, effective venous pressures, initial ventricular pressures, and diastolic stretch of the ventricles greatly exceed those normally operative. As soon as these decrease to normal levels, cardiac output and stroke volumes diminish. Arterial pressures are stabilized for a time due to compensatory vascular mechanisms. This state of myocardial depression continues and is probably intensified during spontaneous circulatory failure which follows infusions, *but it is not the dominant factor responsible for progressive reduction of cardiac output, decline of arterial pressures, and deterioration of pressure pulse patterns.* As after simple hemorrhage, progressive reduction in venous return is the paramount factor. However, coexistence of myocardial depression is certainly not favorable, for it reduces the capacity of the ventricles to expel their diminished blood volumes as effectively as after simple bleeding. Consequently, myocardial depression plays an important role in the rapid downward trend of blood pressure and is the ultimate cause of death.

It cannot be claimed that myocardial depression, similar to that found in our types of experiments, exists in all states of shock. Our evidence does suggest,

however, that a study of myocardial function in shock deserves more careful exploration by cardiologists than has hitherto been given to this aspect of the shock problem. Myocardial depression is a subtle phenomenon and often an occult one even under otherwise normal conditions of the circulation. This is so because compensatory mechanisms operate automatically to maintain normal volumes of systolic discharge and cardiac output. However, as Starling tried so hard to emphasize, such hearts are laboring under a continued strain and nearer to their reserve limit. If, at the time of any shock-producing catastrophe, these reserve mechanisms are already utilized, the superposition of a reduction in venous return after a fairly rapid loss of blood or plasma may be expected to cause an earlier and more rapid development of myocardial depression. Since the functional state of the myocardium and the capacity of coronary response antecedent to shock-producing catastrophies unquestionably vary in dogs as well as in man, it is not surprising that the degree to which myocardial depression contributes to circulatory failure varies considerably. Since cardiodynamic studies have shown that myocardial depression can be a grave subsidiary factor, the problem merits further attention of cardiologists. The possibility that proper cardiac stimulants used in proper dosage and at the proper time may reverse the circulatory failure when transfusions fail to do so should not be regarded as a closed problem.

SUMMARY

The question as to whether myocardial depression occurs in hemorrhagic shock and, if so, its importance was reinvestigated. For this purpose the cardiodynamic changes which occur after simple hemorrhage, during prolonged hypotension (50 to 30 mm. Hg), during reinfusion of all the withdrawn blood, and during spontaneous circulatory failure following infusion, were studied in the same animal. In different series of experiments in which the same standard technique was used, we studied changes in calibrated arterial pressure pulses, cardiac output by a modified Stewart method, alterations in effective venous pressure, ventricular volume and pressure curves, inferior vena cava flow, and electrocardiograms by standard and chest leads.

Following simple hemorrhage sufficient to reduce mean arterial pressure to 50 mm. Hg, the changes in ventricular action are all secondary to reduction in venous return and decrease in effective central venous pressure. Electrocardiograms reveal no significant changes. Changes in the contour of the central arterial pulse consist in abridgement of the period of systolic ejection and development of a primary spike followed by a peaked summit, and this is followed by a deep incisura. As a result of decreased venous pressure, ventricular filling is slower, initial tensions decrease in both ventricles, and their diastolic size is smaller. Pressure and volume curves indicate that the ventricles expel their diminished volumes with good velocity.

If severe posthemorrhagic hypotension is prolonged for 135 minutes, death results from an oligemic type of failure unless blood is reinfused. However, such reinfusion is of only temporary benefit; a slow spontaneous circulatory failure and eventually death follow. Irreversibility develops during the period of pro-

longed hypotension. This includes depression of the myocardium, for while venous return continues to decrease slightly, effective venous and initial ventricular pressures return to or above control levels and the diastolic size of the ventricles augment. Nevertheless, the stroke volume and cardiac output decrease. Myocardial depression is further indicated by a subminimal stroke volume when venous pressures are elevated to normal levels and by development of S-T depression in electrocardiograms.

Reinfusion of blood restores arterial pressures and pulses as well as cardiac output to normal, but in order to do so the ventricles are required to operate under supernormal conditions of high venous pressure and initial tensions. As soon as these re-establish at normal levels, cardiac output decreases, and the ventricles pump less efficiently due to a depressed state of the myocardium. As arterial pressure declines to ca. 70 mm. Hg, reduction in venous return becomes so great that the myocardial depression is obscured but is detectable by special tests. A progressive circulatory failure develops despite the fact that blood volumes are not significantly decreased. This represents a form of *normovolemic shock* due solely to default of the peripheral circulation and of the myocardium. The preduction of venous return is of paramount importance, but circulatory failure is hastened by coexistent myocardial depression.

Since the functional state of the myocardium and the capacity of the coronary responses at the time of shock-producing catastrophies may often be below par, myocardial depression may play as significant a subsidiary role in some cases of human shock as it did in our animals submitted to a particular type of hemorrhage and shock. The problem deserves further careful exploration by cardiologists.

REFERENCES

1. Henderson, Y.: Acapnia and Shock. I. Carbon-Dioxide as a Factor in the Regulation of the Heart Rate, Am. J. Physiol. **21**:126-156, 1908.
2. Henderson, Y.: Acapnia and Shock. VII. Failure of the Circulation, Am. J. Physiol. **27**:152, 1910.
3. Wiggers, C. J.: The Prognostic Significance of Pulse Pressure Changes During Hemorrhage, Arch. Int. Med. **6**:281, 1910.
4. Harkins, H. N.: Recent Advances in the Study and Management of Traumatic Shock, Surgery **9**:231-294, 447-482, 607-655, 1941.
5. Moon, V. H.: Shock: Its Dynamics, Occurence and Management, Philadelphia, 1942, Lea & Febiger.
6. Wiggers, C. J.: The Present Status of the Shock Problem, Physiol. Rev. **22**:74, 1942.
7. Gregersen, M. I.: Shock, Ann. Rev. Physiol. **8**:335, 1946.
8. Howell, W. H.: Shock, Contributions to Medical Research (dedicated to V. C. Vaughan), Ann Arbor, 1903, George Wahr, p. 51.
9. Henderson, Y.: Acapnia and Shock, Am. J. Physiol. **27**: 173, 1910.
10. Erlanger, J., and Gasser, H. S.: Shock Due to Mechanical Limitation of Blood Flow, Am. J. Physiol. **49**: 162, 1919.
11. (a) Kohlstaedt, K. G., and Page, I. H.: Terminal Hemorrhagic Shock, Circulatory Dynamics, Recognition and Treatment, Surgery **16**:430, 1944.
    (b) Mylon, E., Cashman, C. W., Jr., and Winternitz, M. C.: Studies on Mechanisms Involved in Shock and Its Therapy, Am. J. Physiol. **142**:299, 1944.
12. Prinzmetal, M., and Bergman, H. C.: Heart in Experimental Shock, J. Mt. Sinai Hosp. **12**:579, 1945.

13. Meneely, G. R., Stahlman, M., McCrea, F. R., Smith, L. E., and Smith, H. J., Jr.: Ischemic and Anoxemic Damage to Myocardial Capillaries and Its Relation to Shock, Angina Pectoris, and Myocardial Infarction, Federation Proc. No. **5**:226, 1946.

14. Burdette, W. J., and Wilhelmi, A. E.: Respiration of Heart Muscle Slices From Rats in the Terminal Stages of Hemorrhagic Shock, Proc. Soc. Exper, Biol. & Med. **61**:411, 1946.

15. Wiggers, C. J., and Werle, J. M.: Exploration of a Method for Standardizing Hemorrhagic Shock, Proc. Soc. Exper. Biol. & Med. **49**:604, 1942.

16. Huizenga, K. A., Brofman, B. L., and Wiggers, C. J.: The Ineffectiveness of Adrenal Cortex Extracts in Standardized Hemorrhagic Shock, J. Pharmacal. & Exper. Therap. **78**:139, 1943.

17. Wiggers, H. C.: Cardiac Output and Total Peripheral Resistance Measurements in Experimental Dogs, Am. J. Physiol. **140**:519, 1944.

18. (a) Gelfan, S.: Sensitivity to Morphine During Recovery From Hemorrhagic Shock, Federation Proc. **5**:31, 1946.
(b) Powers, S., Reed, C., and Gregersen, M. I.: The Effects of Morphine on Dogs in Hemorrhagic and Traumatic Shock, Am. J. Physiol. **148**:269, 1947.

19. Burstein, C. S., and Hershey, S. G.: Circulatory Effects From Pentothal Sodium Administered Soon After Hemorrhage, Proc. Soc. Exper. Biol. & Med. **53**:80, 1943.

20. Green, H. D., Nickerson, N. D., Lewis, R. N., and Brofman, B. L.: Consecutive Changes in Cutaneous Blood Flow, Temperature, Metabolism, and Hematocrit Readings During Prolonged Anesthesia With Morphine and Barbital, Am. J. Physiol. **140**:177, 1943.

21. Lewis, R. N., Werle, J. M., and Wiggers, C. J.: The Behavior of the Spleen in Hemorrhagic Hypotension and Shock, Am. J. Physiol. **138**: 205, 1943.

22. Ingraham, R. C., and Wiggers, H. C.: Alkalinizing Agents and Fluid Priming in Hemorrhagic Shock, Am. J. Physiol. **144**:505, 1945.

23. de Pasqualini, C. D.: Standardized Hemorrhagic Shock in the Guinea Pig, Am. J. Physiol. **147**:591, 1946.

24. Eckstein, R. W., Graham, G. R., Liebow, I. M., and Wiggers, C. J.: Comparison of Changes in Inferior Cava Flow After Hemorrhage and Circulatory Failure Following Tranfusion, Am. J. Physiol. **148**:745, 1947.

25. Blalock, A.: Mechanism and Treatment of Experimental Shock. I. Shock Following Hemorrhage, Arch. Surg. **15**: 762, 1927.

26. Johnson, G. S., and Blalock, A.: Experimental Shock. IX. A Study of the Effects of the Loss of Whole Blood, of Blood Plasma, and of Red Blood Cells, Arch. Surg. **22**:626, 1931.

27. Shore, R., Holt, J. P., and Knoefel, P. K.: Determination of Cardiac Output in the Dog by the Fick Procedure, Am. J. Physiol. **143**:709, 1945.

28. Wiggers, H. C., and Middleton, S.: Cardiac Output and Total Peripheral Resistance in Post-hemorrhagic Hypotension and Shock, Am. J. Physiol. **140**:677, 1944,

29. Werle, J. M., Cosby, R. S., and Wiggers, C. J.: Observations on Hemorrhagic Hypotension and Hemorrhagic Shock, Am. J. Physiol. **136**:401, 1942.

30. Wiggers, C. J.: The Failure of Transfusions in Irreversible Hemorrhagic Shock, Am. J. Physiol. **144**:91, 1945.

31. Wiggers, C. J., and Werle, J. M.: Cardiac and Peripheral Resistance Factors as Determinants of Circulatory Failure in Hemorrhagic Shock, Am. J. Physiol. **136**:421, 1942.

32. Wegria, R., Guevara Rojas, A., and Wiggers, C. J.: A Study of Spontaneous Fulminant Shock in a Heart-Lung-Dog Preparation, Am. J. Physiol. **138**:212, 1943.

33. Opdyke, D. F., and Wiggers, C. J.: Studies of Right and Left Ventricular Activity During Hemorrhagic Hypotension and Shock, Am. J. Physiol. **147**:270, 1946.

34. Eckstein, R. W., Liebow, I. M., Graham, G., and Wiggers, C. J.: Comparison of Changes in Inferior Cava Flow After Hemorrhage and Circulatory Failure Following Transfusion, Am. J. Physiol **148**:745, 1947.

35. Manrique Izquieta, J., and Pasternack, B.: Electrocardiographic Changes in Hemorrhage and Ischemic Compression Shock. Proc. Soc. Exper. Biol. & Med. **61**:407, 1946.

KENT'S FIBERS AND THE A-V PARASPECIFIC CONDUCTION THROUGH THE UPPER CONNECTIONS OF THE BUNDLE OF HIS-TAWARA

Ivan Mahaim, M.D.*
Lausanne, Switzerland

AT THE end of the last century the "myogenists," who considered cardiac contraction to be a peristaltic wave, still had to do away with one obstacle before seeing the triumph of their conception. The "neurogenists" opposed them with an argument that seemed final: in the heart of man the auricles are separated from the ventricles by an inert conjunctive ring which makes it impossible for the wave of auricular contraction to reach the ventricles.

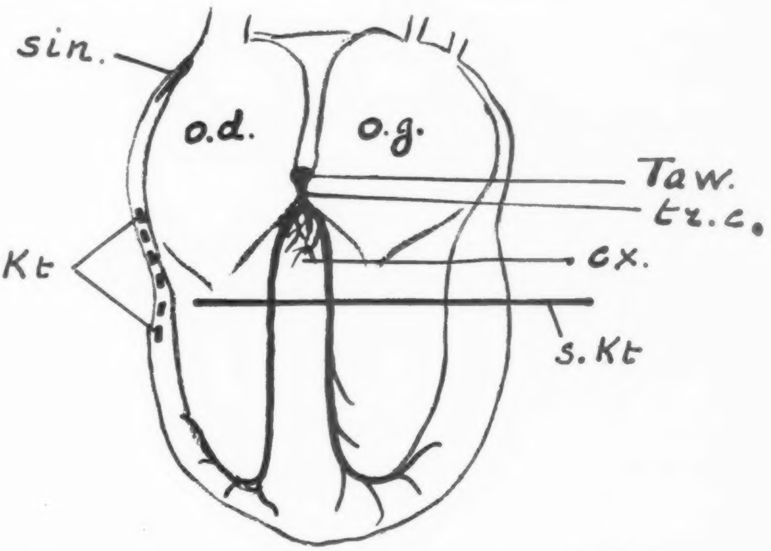


Fig. 1.—Scheme of the bundle of His-Tawara with the node of Tawara, *Taw.*, the main trunk, *tr.c.* and the Kent's fibers, *Kt.* The transverse line, *s.Kt*, represents the experimental section performed by Kent. The upper connections are represented by *cx.*

It was to remove this obstacle that His and Kent sought to discover a muscular bridge, a contractile hyphen between the auricles and ventricles of the human heart. They published their results simultaneously in 1893, independently

Read at the Second Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.
*Privat-Docent of the University of Lausanne.

of one another. His discovered the hyphen in the membranous septum, and what he found corresponds to what is known today as the main trunk of the bundle of His-Tawara. However, it was not until thirteen years later that this discovery came to light in Tawara's monograph (1906). Since then, the bundle of His has been considered as a complete organ consisting of specific tissue and having its particular physiology and pathology.

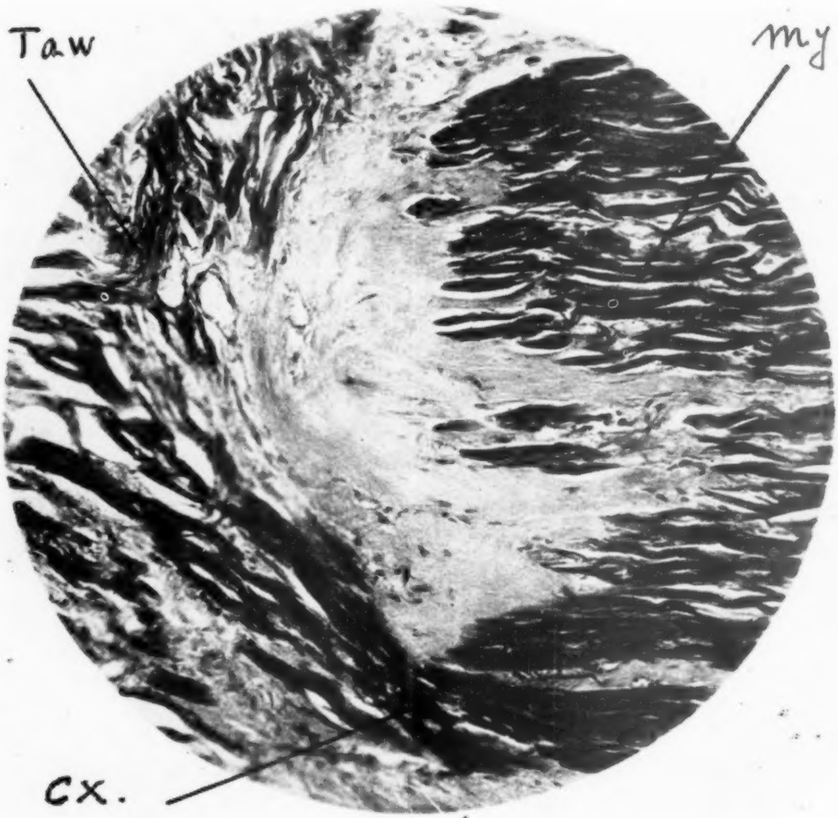


Fig. 2.—Large connection, *cx.*, uniting the node of Tawara, *Taw*, with the myocardial septum, *my*, in man.

Not as much can be said about Kent's fibers, which have never been made the object of a systematic description nor of a monograph. Following his first publication, Kent remained silent for twenty years. In 1913, he returned to the question when he published some few figures and reported certain experimental observations. In the earliest studies the fibers of Kent were represented as being small myocardial fasciculi joining the auricles to the ventricles in the regions of the lateral walls of the heart. In 1913, Kent no longer insisted on the left lateral fibers, but sought to identify a right lateral bundle uniting the right

auricle to the right ventricle. To confirm its function, he carried out a decisive experiment which consisted of severing the heart transversely in the horizontal plane, thus sectioning the interventricular septum with the two branches of the bundle of His-Tawara and leaving intact only the right lateral region (Fig. 1, *s. Kt*) where the so-called right lateral bundle was thought to be located. Kent concluded that, under these circumstances, it was this bundle, and it alone, which permitted a contractile wave to pass from auricles to ventricles.

Kent's experiments are described in a very summary manner. What is more important is that, even though correctly conducted, they were not adequate to resolve the question. When the experiments were made, Kent ignored a cause of error, on which I will present a few precise remarks.

According to the works of Tawara and those of Mônckeberg, it was believed that the main trunk and the two branches were isolated in a conjunctive retaining "muff". In 1932 I described the upper connections which unite the origin of the left branch to the upper part of the interventricular septum. I have found them again with Benatt, and later studied them experimentally with the aid of Rothberger in Vienna. These last findings have been published in detail with Winston (1941). Aschoff and Meesen, finally, have confirmed their existence. Fig. 2 represents one of these connections, particularly large, which unites the anterior and inferior part of the nodes of Tawara to the myocardial septum.

If we consider again the schema in Fig. 1 representing Kent's experiment, we understand without difficulty that the right lateral bundle of Kent is not alone in being able to conduct the wave of excitation from the auricle to the ventricle. This excitation may pass to the two ventricles through the upper connections above Kent's section.

If conduction by Kent's fibers is accepted (and it has still not been proved that these fibers exist regularly, and one can even doubt it), it should be regarded as an accessory form of conduction: paraspecific conduction.

Paraspecific conduction recognizes the contradictions which are manifest in the anatomicoclinical researches on bundle branch block. I will not dwell on this here. It applies, perhaps, also to the syndrome of Wolff-Parkinson-White, as Lequime and his collaborators have suggested.

REFERENCES

1. His, W., Jr.: Die Thätigkeit des embryonalen Herzens unteren Bedeutung für die Lehre von Herzbewegeung beim Erwachsnen, Arb. a. d. med. Klin. zu Leipzig (Vogel), p. 14, 1893.
2. Kent, A. F. S.: J. Physiol. (Cambridge) **14**:233 (Proc. XXIII-XXIV), 1893.
3. Kent, A. F. S.: J. Physiol. (Cambridge) **47**: (Proc. XVII), 1913.
4. Kent, A. F. S.: J. Physiol. (Cambridge) **48**:22 (Proc. XXII), 57 (Proc. LVII), 63 (Proc. LXIII), 1914.
5. Lequime, J., Segers, M., and Denolin, H.: Cardiologia **8**:113, 1944.
6. Mahaim, I.: Ann. de méd. **32**:347, 1932.
7. Mahaim, I.: Compt. rend. Soc. de biol. **109**:183, 1932.
8. Mahaim, I., and Benatt, A.: Cardiologia **1**:61, 1937.
9. Mahaim, I., and Winston, M.: Cardiologia **5**:189, 1941.
10. Meessen, H.: Ztschr. f. Kreislaufforsch. **27**:42, 1935.
11. Mönckeberg, J.: In Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, 1942, Julius Springer, vol. 2.
12. Tawara, S.: Das Reizleitungssystem des Säugetierherzens, Jena, 1906, Gustav Fischer.

THE EFFECT OF SMOKING ON THE VASODILATATION PRODUCED BY THE ORAL ADMINISTRATION OF 95 PER CENT ETHYL ALCOHOL OR A SUBSTANTIAL MEAL

GRACE M. ROTH, PH.D.,* AND CHARLES SHEARD, PH.D.†
ROCHESTER, MINN.

INVESTIGATORS have inquired whether the oral administration of alcohol or the ingestion of a substantial meal will prevent the constriction of peripheral blood vessels known to be produced by the smoking of tobacco. Heberden[1] in 1802 first suggested the efficiency of alcoholic beverages in relief of angina pectoris, perhaps because they seemed to be vasodilators of no mean degree. In 1910 Brooks[2] observed in animals a rise in blood pressure and pulse rate immediately after the ingestion of alcohol with a subsequent lowering of blood pressure and increase of heart rate. In man, Lieb[3] gave not more than 10 c.c. of whisky orally and found only slight changes in the blood pressure and pulse rate and these only after absorption had taken place. Grollman[4] gave 35 c.c. of 95 per cent ethyl alcohol orally to normal persons and observed an increase in the blood pressure, pulse rate, and cardiac output within fifteen to thirty-five minutes after the ingestion of the alcohol. He believed this was secondary to the peripheral vasodilatation.

In 1932, Cook and Brown[5] demonstrated, by measurement of skin temperature of the extremities, that oral administration of 95 per cent ethyl alcohol would produce vasodilatation of the peripheral blood vessels in both normal persons and in some individuals suffering from peripheral vascular disease. This vasodilatation lasted two hours or more. We have demonstrated that a substantial meal would give a similar result.[6,7] We have shown, also, that irrespective of existing vasodilatation from the oral administration of alcohol, the degree of vasoconstriction induced in the usual cold pressor test was not altered significantly.[8] With this background, we set out to try to answer the query of investigators with which this presentation opened.

PROCEDURE

The measurement of vasoconstriction and vasodilatation of the extremities was made by determination of the skin temperature of the fingers and toes, together with simultaneous observations of blood pressure and pulse rate.

Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.
*From the Section on Clinical Physiology, Mayo Clinic.
†Division of Physics and Biophysical Research, Mayo Foundation.

The observations were made on sixty-five normal persons, six women and fifty-nine men, whose ages ranged from 19 to 59 years, and whose basal metabolic rates ranged from −21 to +5 per cent. Many of them were physicians. All were habitual smokers and inhaled the smoke.

Data were obtained in a room in which the constant temperature was 25.5° C. (78° F.) and the relative humidity was 40 per cent. The subjects fasted for fifteen hours before the tests and, during the tests, they wore lightweight short pajamas and lay supine on comfortable beds.

The temperature of the plantar surfaces of the first and third toes of both feet and the volar sides of the distal phalanges of the first and third fingers of both hands were measured by means of thermocouples of copper and constantan. Generally, after a control period of about an hour, when fairly constant readings of the cutaneous temperature had been obtained and determinations of basal blood pressure and pulse rate had been made, smoking was begun. Two-thirds of two cigarettes of a standard brand were smoked in succession. Simultaneous determinations of blood pressure, pulse rate, and cutaneous temperature were obtained at intervals of one minute during the smoking, which generally lasted about twelve to sixteen minutes. The subjects inhaled the smoke at the depth and frequency customary with them. An attempt was made to eliminate all unnecessary noise and other stimuli which might produce vasoconstriction during this period. The procedure described established whether the subjects' blood vessels became constricted during smoking and, if so, to what degree.

On the same day that this preliminary test of the effects of smoking had been completed, or on another day shortly thereafter, 30 c.c. of 95 per cent ethyl alcohol in 250 c.c. of fruit juice was administered by mouth. After vasodilatation had become evident as an increase of the skin temperature of the toes and fingers, the subjects smoked two-thirds of two cigarettes. During the smoking, blood pressure and pulse rates were noted at intervals of one minute, as previously.

The same procedure was followed before and after the taking of a substantial meal.

RESULTS

One hundred twenty-one tests were made on the sixty-five subjects; in eighty-seven of these tests alcohol was employed, while in thirty-four food was used. Some of the same subjects were given food at one time and alcohol at another.

In one subject smoking before the ingestion of alcohol produced a considerable increase in the pulse rate, a small but definite increase in both systolic and diastolic blood pressure, and a definite decrease in the skin temperature of the fingers and toes. The decrease in the skin temperature was greater in the toes and of longer duration (Fig. 1).

Forty minutes after the ingestion of alcohol, evidence of vasodilatation was present and smoking was repeated. The effect was similar to that of smoking before the ingestion of alcohol except that the skin temperature of the toes and fingers did not decrease (Fig. 1). This observation indicates at least partial

inhibition by the alcohol of the vasoconstriction ordinarily produced by smoking. This result; however, was obtained in only one of the sixty-five subjects and this one had a basal metabolic rate of +1 per cent.

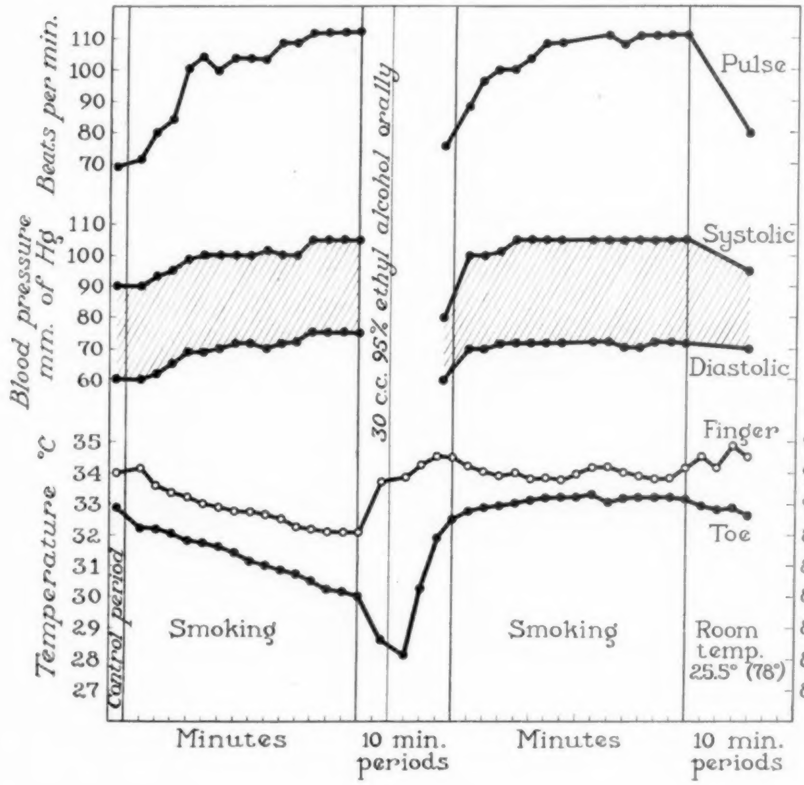


Fig. 1.—The effect of smoking two standard cigarettes, alone and after the ingestion of 95 per cent alcohol, on the skin temperature of the extremities, blood pressure, and pulse rate of the same subject. The skin temperature curves of only one toe and one finger are shown. The control period was sixty minutes. The skin temperature of the fingers and toes failed to decrease on smoking after the ingestion of alcohol. This was an unusual response.

Another subject had evidence of greater vasoconstriction of the blood vessels of the extremities (Fig. 2) than that of the normal subject just mentioned. On smoking before the ingestion of alcohol, the blood pressure and pulse rate of this second person increased definitely. The skin temperature of the toes decreased 5.0° C. and that of the fingers 5.3° C. (Fig. 2). These effects were still evident fifty minutes after the ingestion of alcohol. At that time there was only slight vasodilatation of the toes, for the skin temperature did not approximate the pre-smoking basal level.

On smoking after the taking of alcohol, the skin temperature of the toes of this second subject decreased only 2.5° C. but reached the same level as that which was obtained on smoking before the ingestion of alcohol. The skin temperature of the fingers decreased only 1.5° C. in contrast to 5.3° C. before alcohol. The small decrease of 1.5° C. in the skin temperature of the fingers was the exception instead of the rule, since it occurred in only five subjects of the entire group. The rise in blood pressure and pulse rate was similar to that which occurred following smoking alone.

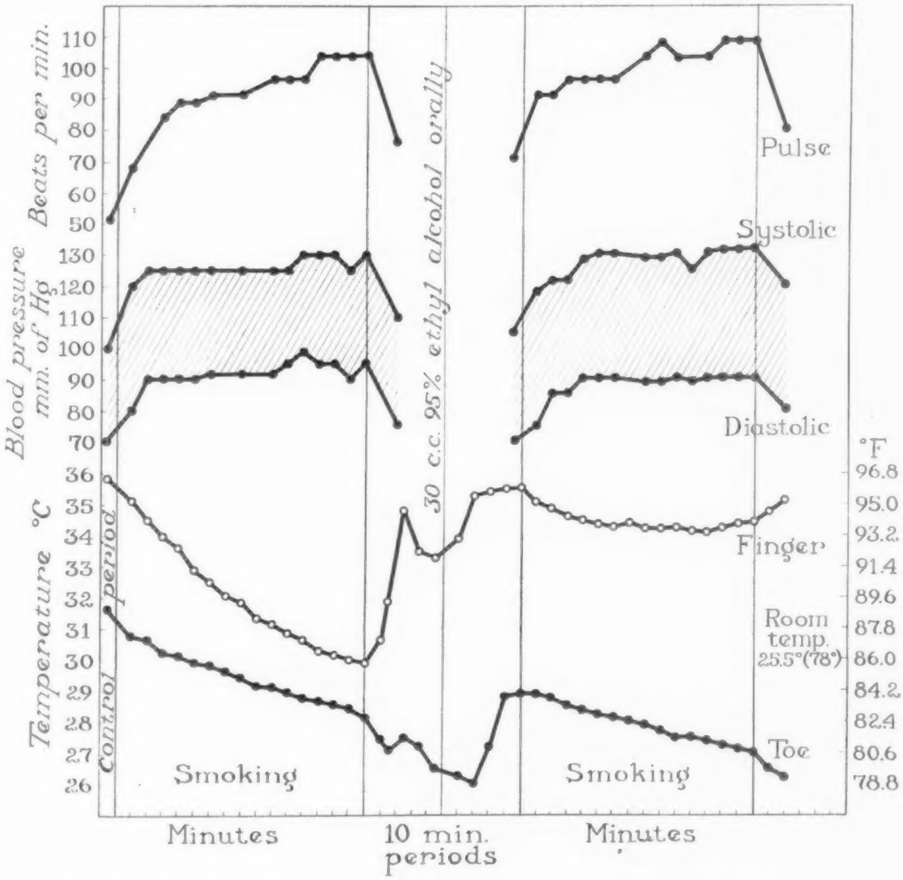


Fig. 2.—The effect of smoking two standard cigarettes, alone and after the ingestion of 95 per cent ethyl alcohol, on the skin temperature of the extremities, blood pressure, and pulse rate of the same subject. The skin temperature of the toes decreased after smoking and failed to return to basal levels in fifty minutes after the ingestion of alcohol.

In many instances the effect of smoking immediately before the ingestion of alcohol persisted and caused us to delay until the following day the test of smoking after ingestion of alcohol.

The more usual effect of smoking after ingestion of alcohol which was experienced by 72 per cent of the subjects tested is demonstrated in Fig. 3. The skin temperature of the toes decreased below the basal level obtained before smoking or the ingestion of alcohol.

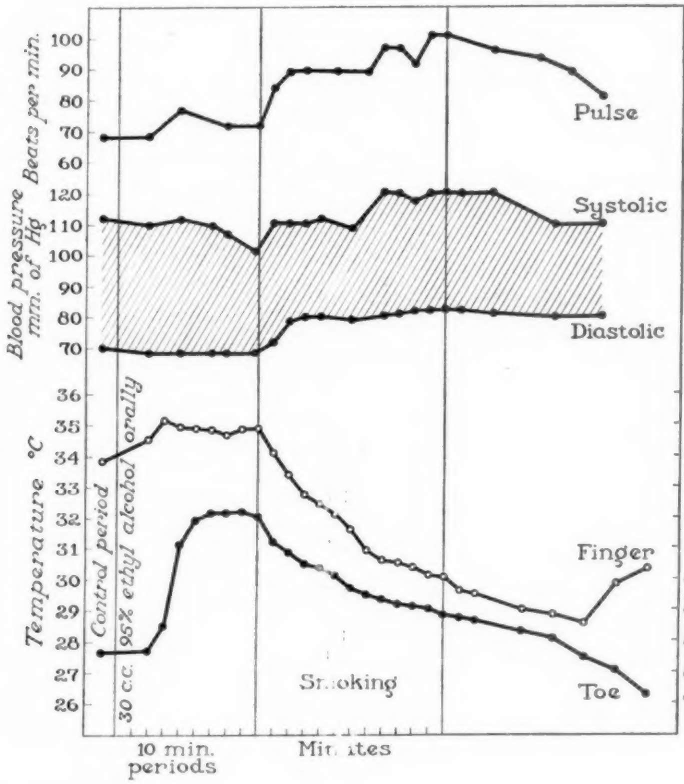


Fig. 3.—The effect of smoking two standard cigarettes after the ingestion of 95 per cent ethyl alcohol on the skin temperature of the extremities, blood pressure, and pulse rate. This was the typical response to smoking.

Results of tests of smoking after the taking of food on two subjects when the control test had been performed the previous day are shown in Fig. 4. The decrease in the skin temperature of the fingers and toes was less in the first individual, whose basal metabolic rate was +1 per cent, than in the second individual, whose basal metabolic rate was −8 per cent. This variation in results shows the correlation of the skin temperature of the toes to the basal metabolic rate. The decrease of the skin temperature of the fingers and toes of the second individual on smoking after the taking of food was similar to that found in many individuals on smoking after ingestion of alcohol. In only four of the tests of smoking after a meal did the skin temperature of the toes remain above the basal

level that existed before eating and that of the fingers remained above the basal level in only two tests. The usual increase of the pulse rate and blood pressure on smoking was noted also on smoking after ingestion of food. This was slightly greater in the second individual, whose test is shown in Fig. 4, than in the first.

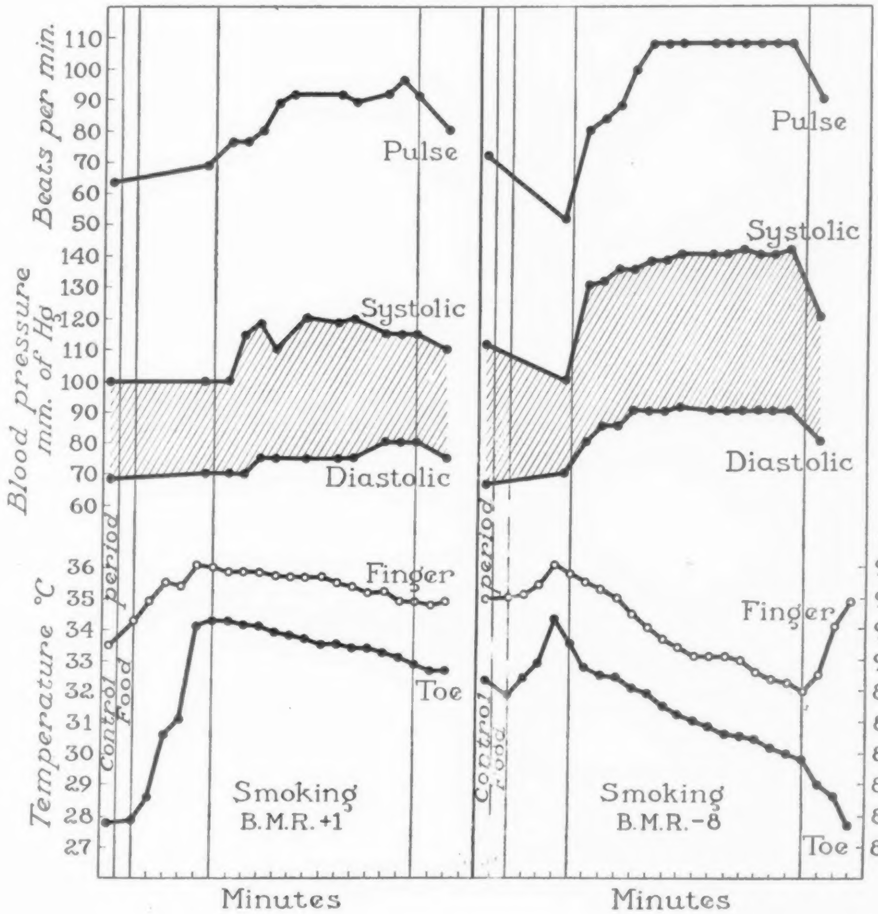


Fig. 4.—The effect of smoking two standard cigarettes after the ingestion of a substantial meal. The difference in behavior of the skin temperature of the fingers and toes with the difference in basal metabolic rate may be noted.

When the physiologic effects of smoking on all subjects were analyzed statistically, the average increase in blood pressure which followed smoking alone was 6 mm. Hg systolic and 5 mm. Hg diastolic more than that which followed smoking after the previous ingestion of alcohol (Fig. 5). When the subjects smoked before the ingestion of food the average systolic pressure was 1.4 mm. lower and the diastolic was 3 mm. higher than when they smoked after the ingestion

of food. These differences, however, could not be considered significant. Likewise, the average differences in the pulse rates on smoking before and after the ingestion of alcohol or food were not significant.

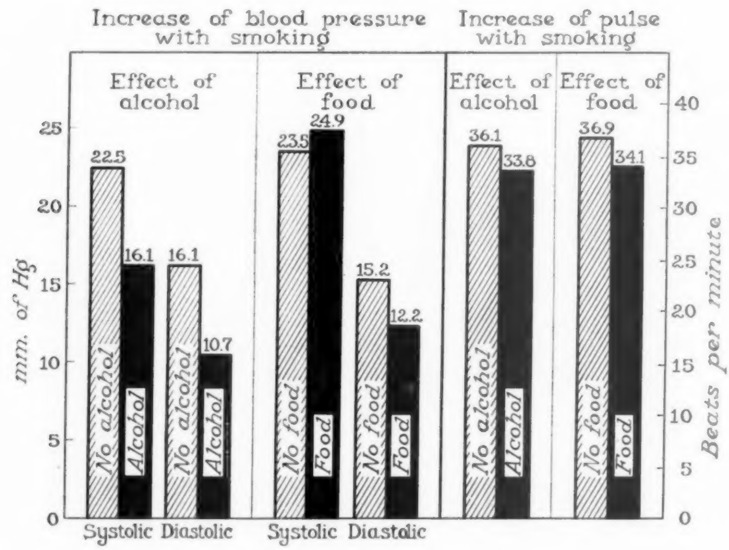


Fig. 5.—The effect of smoking two standard cigarettes on the blood pressure and pulse rate of all subjects before and after the ingestion of alcohol or a substantial meal.

The differences in the average skin temperature of the toes and fingers are shown in Table I. After smoking alone, the average decrease of the skin temperature of the toes in the group in which alcohol was used later was 2.1° C., with a range of 0.8 to 5.2° C., while the average temperature of the fingers decreased 3.0° C., with a range from 0.8 to 6.0° C.

When the subjects smoked after taking alcohol, the average skin temperature of the toes returned to the basal level and there was a decrease of only 1.3° C. in the skin temperature of the fingers. This would seem to indicate that alcohol had prevented the vasoconstriction produced by smoking. However, in 72 per cent of the subjects the skin temperature of the toes was lower than the basal level when smoking was done after ingestion of alcohol. Those who must interpret quantitative results in this field will wish to note the values which indicate definite vasoconstriction as compared with the values at the height of vasodilatation. The decrease shown is of about the same magnitude as that encountered after smoking without the subject's having taken alcohol previously. The same is true for the effects of smoking before and after ingestion of a substantial meal.

TABLE I. MEAN SKIN TEMPERATURE

	DEGREES, CENTIGRADE			
	SMOKING WITHOUT ALCOHOL*		SMOKING WITHOUT FOOD*	
	TOES	FINGERS	TOES	FINGERS
Basal	28.5	33.4	28.5	33.5
Smoking	26.4	30.4	26.5	30.6
Difference	–2.1	–3.0	–2.0	–2.9
	SMOKING AFTER ALCOHOL*		SMOKING AFTER FOOD†	
Basal	28.0	33.4	27.9	32.4
Smoking	28.0	32.1	27.8	31.8
Difference	0.0	–1.3	–0.1	–0.6
At height of vasodilation	30.5‡	34.3‡	29.9§	34.3§
Smoking	28.0	32.1	27.8	31.8
Difference	–2.5	–2.2	–2.1	–2.5

*Probable errors vary from 0.1 to 0.4.
†Probable errors vary from 0.4 to 0.7.
‡From alcohol.
§From food.

COMMENT

The vasodilatation which follows ingestion of alcohol does not take place immediately but only after sufficient absorption of the alcohol has occurred. Therefore, the height of vasodilatation may not be reached until fifty to sixty minutes after the ingestion of alcohol but, once the height has been reached, it persists for one to one and one-half hours. Smoking tests, made at periods varying from thirty to ninety minutes after ingestion of alcohol or ingestion of food, demonstrated that vasoconstriction from smoking could not be prevented by the alcohol or food at any time during vasodilatation from alcohol or food.

The amount of 95 per cent ethyl alcohol used in this study is equivalent to 2 ounces (60 c.c.) of whisky. When either 30 c.c. of 95 per cent ethyl alcohol or 2 ounces of whisky are given after fasting, definite vasodilatation of the peripheral blood vessels occurs. Intoxicating doses of alcohol were not used. It would seem that, under the circumstances of the present study, alcohol is not uniformly an effective agent for the prevention of the vasoconstriction produced by smoking. Therefore, this study does not substantiate the common belief that drinking a cocktail will necessarily nullify the effect of smoking.

REFERENCES

1. Heberden, William: Commentaries on the History and Cure of Diseases, London, 1802, T. Payne, 367 pages.
2. Brooks, Clyde: The Action of Alcohol on the Normal Intact Unanesthetized Animal, J.A.M.A. **55**:372, 1910.

3. Lieb, C. C.: The Reflex Effects of Alcohol on the Circulation, J.A.M.A. **64**:898, 1915.
4. Grollman, Arthur: The Influence of Alcohol on the Circulation, Quart. J. Stud. on Alcohol **3**:5, 1942.
5. Cook, E. N., and Brown, G. E.: The Vasodilating Effects of Ethyl Alcohol on the Peripheral Arteries, Proc. Staff Meet., Mayo Clin. **7**:449, 1932.
6. Sheard, C., Williams, M., Roth, G. M., and Horton, B. T.: The Role of the Extremities in the Dissipation of Heat From the Body in Various Atmospheric and Physiological Conditions, Tr. Am. Soc. Heating & Ventilating Engineers **45**:135, 1939.
7. Sheard, Charles: Temperature of Skin and Thermal Regulation of the Body, In Glasser, Otto: Medical Physics, Chicago, 1944, The Year Book Publishers, Inc., pp. 1523-1555.
8. Roth, Grace M., and Sheard, Charles: The Effect of Peripheral Vasodilatation on Vasoconstriction: Determinations Made on the Basis of Blood Pressure of Normal Subjects, Am. J. Physiol. **137**:695, 1942.

REPORT FROM THE CARDIAC CLINIC OF THE BOSTON LYING-IN HOSPITAL FOR THE FIRST TWENTY-FIVE YEARS

BURTON E. HAMILTON, M.D.
BOSTON, MASS.

A CARDIAC clinic at the Boston Lying-in Hospital was started under my direction in 1921. During the twenty-five years, 76,125 women have been treated by the hospital through pregnancy; 1.8 per cent of the total, namely, 1,335, pregnancies occurred in women with heart disease. The maternal death rate for these cardiac patients for the twenty-five years was 3.9 per cent.

Three years after the cardiac clinic started, the maternal death rate for the cardiac patients dropped from nearly 20 per cent to less than 5 per cent. In three-year periods since then, the rate has always been below 5 per cent, and usually less than 3 per cent. The drop in maternal mortality of cardiac patients has been accompanied by a drop in maternal mortality in general. The cardiac mortality, however, dropped suddenly in 1923 when modern methods for the control of our cardiac patients were made effective. Improvement in general maternal mortality has been by lysis and spreads over many years. This drop in the maternal mortality of cardiac patients indicates that for women with chronic rheumatic heart disease, *treatment*, not the vagaries of rheumatic fever, is the largest factor in the prognosis for pregnancy. It supports a belief based on long experience that treatment is the biggest factor in the whole course of young adults with rheumatic heart disease.

For the first fifteen years of the cardiac clinic, the cardiac patients contributed 14 per cent of all maternal deaths; for the last ten years, 28 per cent. *As the general maternal death rate falls, the small number of women with chronic complicating disease becomes relatively more important in determining general maternal mortality.* This fact should be taken into account by those interested in maternal and infant welfare.

The 1,335 pregnant cardiac patients include:

1,244 with chronic rheumatic heart disease	93. %
69 with congenital cardiovascular defects	5.2%
22 with miscellaneous cardiovascular diseases, including cardiovascular syphilis (only 3 cases), thyroid heart, acute pericarditis, etc.	1.8%

One and six-tenths (1.6) per cent of all the pregnancies were in patients with *rheumatic heart disease.* Their maternal death rate was 3.8 per cent.

Read at the Second Inter-American Congress of Cardiologists in Mexico, D. F., Oct. 5-12, 1946.

Those with rheumatic heart disease are subdivided into favorable and unfavorable cases. The definition of a favorable case for pregnancy is a woman with mimimal (or more than minimal) signs of rheumatic heart disease who is able to carry on moderate activity without having heart failure and who has no complicating condition which is in itself dangerous, such as essential hypertension, chronic bronchitis, diabetes.

On this basis, the maternal mortality for favorable cases for approximately the first fifteen years at the cardiac clinic was 2.5 per cent. The infant mortality was 12 per cent. For the unfavorable patients, the maternal mortality was 16 per cent and the infant mortality 46 per cent.

During the last ten years, the maternal mortality for the favorable cases has been only 2 per cent and the infant mortality 8.6 per cent. The maternal mortality, however, in the unfavorable cases remains high, namely, 18 per cent; the infant mortality has dropped to 31 per cent.

During the period that these statistics cover, the yearly death rate for women between the ages of 20 and 40 years in the region of Boston was approximately 0.45 per cent. During the last ten years, the yearly death rate for my private women patients between the ages of 20 and 40 years with rheumatic heart disease who were favorable cases by the criteria given was exactly the same as the death rate at the Boston Lying-in Hospital for similar cases in pregnancy. On the other hand, the *yearly* death rate for my women patients with rheumatic heart disease between the ages of 20 and 40 years who were unfavorable cases was only 6.7 per cent, while the death rate in pregnancy for similar cases at the Boston Lying-in Hospital in the last ten years was 18 per cent. Only twenty-two of those with rheumatic heart disease were found to have *auricular fibrillation* at any time during pregnancy and puerperium; 32 per cent of those with auricular fibrillation died. The infant mortality was approximately 50 per cent. I have found the yearly mortality among comparable nonpregnant women who have auricular fibrillation to be 8 per cent.

A pregnancy, then, has cost the favorable cases little, if any, more risk than their risk of death in one year of living, but it has cost the unfavorable cases a risk nearly three times greater, and those that have auricular fibrillation, a risk that is four times greater.

Individual patients, of course, are more or less favorable and more or less unfavorable. In the Boston Lying-in Hospital cardiac clinic, patients under 23 years of age are, roughly, ten times as liable to recurrences of rheumatic fever as are the older ones. Those who are over 35 years of age are twice as liable to congestive heart failure as are the younger ones. Those with markedly enlarged hearts do not do so well as those that have only slight enlargement. Maternal mortality for those that have mitral stenosis, or aortic regurgitation, or both, is nearly the same, but those who have enlargement of the heart and a systolic murmur (only 6 per cent of those with a diagnosis of rheumatic heart disease) have had a materially lower maternal mortality. Though the maternal mortality is higher for primiparas and those who have had multiple pregnancies than it is for those who are para ii, iii, or iv, these discrepancies can be best accounted for

by factors other than parity; namely, the patient's favorable or unfavorable cardiac status and the patient's age.

It is on these data that we base advice and information given to patients with rheumatic heart disease who are contemplating pregnancy.

The causes of all the maternal deaths among the cardiac patients were:

Congestive heart failure	39%
Bacterial endocarditis	20%
Embolism	15%
Miscellaneous*	26%

The causes of maternal death among favorable cardiac patients were:

Congestive heart failure	12%
Bacterial endocarditis	35%
Embolism	16%
Miscellaneous*	37%

The causes of maternal death among unfavorable cardiacs patients were:

Congestive heart failure	64%
Bacterial endocarditis	7%
Embolism	13%
Miscellaneous*	16%

Congestive heart failure caused two-thirds of the deaths among the unfavorable cases, but only 12 per cent of the deaths among the favorable cases. It seems that among cardiac patients, maternal deaths from congestive heart failure would be extremely rare (one in 417 cases) if patients with an unfavorable cardiac status avoided pregnancy. (Many of the patients with an unfavorable cardiac status, however, for one reason or another, desired pregnancy greatly and became pregnant in full knowledge of their danger. It is certainly not to be expected and probably not desirable that all of them avoid pregnancy.)

Among the favorable cardiac patients, 35 per cent of the maternal deaths were attributable to bacterial endocarditis. We hope for fewer deaths from this cause, but there will be more women "cured" of bacterial endocarditis who will later become pregnant and we are not certain of their prognosis for pregnancy.

The maternal mortality of the 69 patients with *congenital cardiovascular defects* was 2.9 per cent.

Patients with *patent ductus arteriosus* (including a few who had had the ductus ligated before pregnancy) have done very well in pregnancy.

There have been no maternal deaths among those with *coarctation of the aorta*, and the infant mortality was satisfactory. Some individuals, however, have had alarming symptoms.

Several of the few with a diagnosis of *ventricular septal defect* have had serious circulatory symptoms after delivery, and there has been one maternal death (another among my private patients).

*Miscellaneous includes deaths from sepsis, "toxemias," hemorrhage, pneumonias, acute appendicitis.

One previously reported patient with the tetralogy of Fallot, severe cyanosis, and drumstick fingers survived six pregnancies with much difficulty, most of this directly after delivery. Only one of the infants survived.

Patients with *essential hypertension* are not analyzed carefully in this report because (1) difficulty in differentiating essential hypertension from hypertension attributable to the "toxemias of pregnancy" and (2) lack of methods for clear subclassification of those that can be confidently diagnosed essential hypertension have prevented the accumulation of large numbers of accurately diagnosed patients. Small numbers of carefully diagnosed patients have been followed. From them we suspect, but cannot prove, that women with mild essential hypertension do as well as the favorable cardiac patients and that those with severe cases do somewhat better than the unfavorable cardiac patients. We suspect, however, though we cannot prove it, that pregnancy tends to hasten the progress of essential hypertension.

In addition to the statistics that the heart clinic has produced in twenty-five years, the following experiences seem to be most noteworthy:

1. The abrupt drop in maternal mortality of the whole group of cardiac patients coincident with the introduction of modern methods for their care (discussed previously).

2. Determination by direct study of the extent of many of the physiologic changes in the circulation attributable to normal pregnancy. The curve of the average load of normal pregnancy on the circulation indicates that the load is small until the sixth calendar month, when it rises steeply to roughly 50 per cent above normal and, on the average, maintains this level until the last calendar month, when it falls off until term. This fall amounts to approximately half the greatest rise. (This is consistent with the fact that congestive heart failure among the cardiac patients is common in the seventh and eighth months and seldom occurs *for the first time* in the ninth month or, indeed, at delivery or afterward.) This lightening of the load in the last month of pregnancy has led to a general principle that patients with severe heart disease, whether they have had or are in congestive failure, are not to be interrupted *for cardiac reasons* after the load on the circulation has once grown heavy (approximately at the sixth month). This is a major change in former obstetric practice. Before the late lightening of the load was determined, it was the custom to deliver patients with severe cardiac difficulty by hysterotomy between the thirty-fourth and the thirty-eighth week of pregnancy, when the child was supposed to be viable, in order to spare the mothers the last of the supposed steadily increasing burden of pregnancy. I believe that the mothers have done better, and certainly the infant mortality has improved, since the present rule was adopted. As a result of this rule, the number of hysterotomies done for cardiac reasons has diminished greatly. Now that interference before term is rare, the cardiac patients are allowed to go into labor and are delivered from below unless there is an indication for hysterotomy that is not related to the heart disease.

Familiarty with the curve of the average load of pregnancy on the circulation is a guide to the cause of failure of a heart. If heart failure occurs before

the heavy rise in the load, or, for the first time, after the load has diminished, normal pregnancy does not account for the failure. There is some complication.

Though there is always a great increase in the load in the last trimester, and always a lightening of the load before term, the load in individuals does not always follow the average curve closely. Some delay the rise into the seventh month; others show the decline before the last month. It is, therefore, impossible to predict accurately how any cardiac patient will behave during pregnancy. It is essential to observe each one closely at frequent intervals. (In the cardiac clinic, patients are examined at least once each week throughout pregnancy.)

NEED FOR CONTINUED STUDY OF THE CIRCULATION IN NORMAL PREGNANCY AND OF SEVERAL NEW CARDIAC PROBLEMS

It is clear from the foregoing statistics that, by modern methods, we cannot expect to make pregnancy much safer for the unfavorable cardiac patients. Their maternal mortality during the last ten years (18 per cent maternal mortality with 64 per cent of the deaths from congestive failure) is even higher than it was ten to twenty-five years ago. The only apparent way to improve this situation is to make pregnancy itself a lighter burden.

Increase in circulating blood volume in normal pregnancy appreciably dilutes the blood. The consequent hurried circulation is not economical. The general edema which is common in pregnancy is sometimes accompanied in normal women by dyspnea and pulmonary edema. The blood dilution and the edema are not well controlled by sodium and fluid restriction, vitamins, and high protein intake; and, so far, our attempts to control the edema by hormone administration have not been successful. It seems that there is some not yet discovered factor that is peculiar to pregnancy. It does not seem unreasonable to hope that this factor can be discovered and controlled if there is vigorous work on the problem. Possibly some of the edema and blood dilution could be controlled by more skillful hormone administration, as is suggested by reports of results from the use of hormones in pregnancy in diabetic patients. Possibly there is a toxin that can be controlled which causes some of the undesirable circulatory changes in pregnancy, as is suggested by the reports of O. Watkins Smith and George Van S. Smith on toxin found in menstrual discharge of women.

A small but important subgroup of women with mitral stenosis can be distinguished. There is little information concerning this group. Without known distinguishing symptoms, they develop sudden, usually apparently unprovoked, severe pulmonary congestion, often with hemoptysis, which often amounts to a hemorrhage. Where there is an apparent provoking cause, the severity of the failure is totally out of proportion to the provocation. Though such symptoms occasionally occur in men with mitral stenosis and in women with mitral stenosis who are not pregnant, and they are rare even in pregnancy, they are much more common in pregnant women than in women who are not pregnant, or in men. These patients cannot be recognized by any method that I know of before pregnancy. Their alarming symptoms may appear early in pregnancy before the

load has grown heavy. So far, those that I have observed have always recovered from their first failure, but in every case they have continued to have recurrences of their violent failure, no matter how carefully the heart failure was treated. Two patients that I know of have died in their second attack. Interruption of pregnancy has *always* been followed by cessation of the attacks or great reduction in their frequency, though they may return months or years later. The pregnancy is a heavy factor in production of the symptoms but the course of the symptoms cannot be explained by any known circulatory phenomena of normal pregnancy. Perhaps the provocation for the attacks is hormonal or toxic disturbance, not yet determined, and peculiar to pregnancy.

Several *new problems of the heart in pregnancy* have appeared in the last few years:

1. Patients with tetralogy of Fallot are extremely rare in a cardiac clinic in a lying-in hospital. The recently introduced successful operation for amelioration of this disease should, in time, bring more cases to obstetric clinics.

2. Subacute bacterial endocarditis, before the introduction of treatment with penicillin, accounted for approximately a third of the maternal deaths in the favorable rheumatic heart disease group. Though a few such patients before the introduction of penicillin treatment bore living children, and a very few cured cases have been reported, all of the women whom I have treated during the last twenty-five years, who were found to have subacute bacterial endocarditis during pregnancy, are dead. Unfortunately, this includes two that have been treated at the Boston Lying-in Hospital since the introduction of penicillin therapy. The infants both died. From questionnaires to obstetricians and cardiologists, reports have been received of seventeen women treated for subacute bacterial endocarditis with penicillin during pregnancy or puerperium. Six of the women died during pregnancy, a maternal mortality of 35 per cent. During the five months following delivery, three more of these women died. This gives a maternal mortality of 53 per cent. The fetal mortality was approximately 24 per cent.

3. Prognosis for future pregnancies for a patient who has recovered from subacute baterial endocarditis, under penicillin treatment, is an almost completely new problem. Eleven women (two of them in the Boston Lying-in Cardiac Clinic) who have been "cured" of subacute bacterial endocarditis have *all survived* a pregnancy. Three of them were aborted. Six of the eleven had living children. Since such cases are not common, and the need for information on their outcome is apparent, it is suggested and hoped that cardiologists will send information on such cases that they may encounter to the Boston Lying-in Hospital Cardiac Clinic. Information on data thus obtained can be had whenever requested from this clinic.

PHYSIOLOGIC CONDITION OF THE HEART IN THE NATIVES OF HIGH ALTITUDES

ANDRES ROTTA, M.D.*
LIMA, PERU

WHEN the physiologic characteristics of those who live in high altitudes are studied, we observe several functional and morphologic variations which distinguish them, without racial considerations, from the normal subject who lives at sea level. The present study was made at 4,540 meters above sea level; the barometric pressure is 446 mm. Hg and the tension of oxygen in the atmospheric air is 80.5 mm. of mercury. The principal physiologic characteristics that have been studied by different authors show the following interesting aspects.

Respiratory Apparatus.—There is a wide thorax with an emphysematous shape and an enlarged lung capacity at the expense of the complementary air and of the residual air.[1] Dissociation curve of hemoglobin deviates toward the right, corresponding to a tendency to acidosis.[2]

Blood.—The chief findings are polycythemia with more than six or seven million erythrocytes per cubic millimeter; arterial saturation of 81 per cent; 16.5 Gm. of hemoglobin per 100 c.c. of blood; blood volume equal to 120 c.c. per kilogram of body weight with a slight reduction of plasma; more or less pronounced reticulocytosis; and a slight increase in the blood viscosity.

Tissue Respiration.—One of the interesting observations is an increase of the myohemoglobin, especially in the muscles of permanent activity such as the diaphragm and the heart. Since most changes are a manifestation of exaggerated function, it is of interest to determine whether they represent overwork or whether the different organs have acquired a supercapacity, the apparent physiologic effect being a result of a genuine process of adjustment to altitude.

The purpose of this study is to determine the place of the cardiac muscle in relation to this problem. To accomplish this, the data that have been obtained through x-ray, radioscopic, and electrocardiographic studies, and through other means of physiologic investigation, will be analyzed.

FINDINGS

Radiologic Determination of the Size and Shape of the Heart.—The effects of chronic or permanent anoxia upon the heart have been the object of experimental

Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.
*Associate Professor of Circulatory Physiopathology, School of Medicine, Lima.

studies and of casual and sporadic observations.[5-10] Investigations based upon x-ray study of the heart were made by us in 1938[11] and in 1944 by Miranda and Rotta[12] and by Kerwin.[13] The data presented in the several published papers have all shown an increase of the cardiac dimensions, but it has not been determined if this increase is contributed by all chambers, or if it is the result of a predominant enlargement of one of the heart cavities. It has not been specified either if the increased size of the heart in man is determined by dilatation or hypertrophy of the heart muscle.

In the present work we have analyzed all the data obtained in 400 teleradiograms of healthy adult subjects who had lived all their lives, or at least for several years, at an altitude of 4,540 meters above sea level. In a group of thirty of them, special examinations were carried out.

In the teleradiograms the transverse diameter and the frontal area of the cardiac silhouette were measured and compared with the normal values for subjects of the same weight and height. The tables and nomograms of Ungerleider and Clark[14] and of Ungerleider and Gubner[15] were used. The results are shown as the percentage of deviation from the normal values, considering as an increase any deviation of more than 10 per cent. For comparative purposes the same determinations were made on teleroentgenograms of more than 200 normal subjects with the same racial characteristics who lived at sea level.

The results demonstrate that the transverse diameter was increased in 69.5 per cent of the cases. The increase was between 11 per cent and 45 per cent, with an average increase of more than 19.5 per cent. In 30.5 per cent of the x-ray films, the transverse diameter was within the normal limits accepted by Ungerleider and Gubner and those found by us in persons living at sea level. The frontal area of the cardiac silhouette, determined by planigraphy, was increased in 67.0 per cent of the cases. The average increase was more than 21.3 per cent, with variations between +11 per cent and +49.0 per cent above the normal values. These figures are greater than those given by Kerwin[13] who worked at the lesser altitude of 3,600 meters above sea level while we worked at an altitude of 4,540 meters. In Table I we have summarized the results of these determinations.

In 47 per cent of the frontal x-ray films there was definite prominence of the pulmonary conus, and in 25 per cent of the same films there was a well-defined increase of the right lateral border of the cardiac shadow.

In eighty individuals in whom there was an increase of the transverse diameter and of the area of the cardiac silhouette, a radioscopic study of the heart was made, in anterior as well as in right and left anterior oblique positions. In fifty-two of these subjects (65 per cent), well-defined signs of predominance of the right side of the heart were found, such as pronounced anterior arch with a diminished retrosternal space in the right anterior oblique position, disappearance of the normal concavity of the left border, and enlargement of the left side of the silhouette, features that have been pointed out by Schwedel[16] to be manifestations of enlargement of the right cavities. Moreover, in a great percentage of the x-ray films, there could be seen enlargement of the hilar shadows due to congestion of the pulmonary arteries as well as some congestion of the pulmonary vascular network.

TABLE I. VARIATIONS OF TRANSVERSE DIAMETER AND FRONTAL AREA OF HEART IN 400 INDIVIDUALS LIVING AT 4,540 METERS AND 200 INDIVIDUALS LIVING AT 200 METERS ABOVE SEA LEVEL; FIGURES EXPRESSED AS PERCENTAGES OF DEVIATION FROM NORMAL VALUES, CALCULATED ACCORDING TO THE NOMOGRAMS OF UNGERLEIDER AND CLARK[14] AND UNGERLEIDER AND GUBNER[15]

PERCENTAGE OF DEVIATION FROM NORMAL VALUES	TRANSVERSE DIAMETER				FRONTAL AREA			
	SEA LEVEL		ALTITUDE		SEA LEVEL		ALTITUDE	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
−19 to −15	—	—	—	—	2	1.0	—	—
−14 to −10	2	1.0	—	—	4	2.0	2	0.5
− 9 to − 5	29	14.5	3	0.75	14	7.0	8	2.0
− 4 to 0	61	30.5	10	2.5	43	22.5	21	5.25
+ 1 to + 5	64	32.0	42	10.5	58	29.0	47	11.75
+ 6 to +10	36	18.0	69	17.25	47	23.5	54	13.5
+11 to +15	7	3.5	90	22.5	18	9.0	82	20.5
+16 to +20	1	0.5	84	21.0	10	5.0	80	20.0
+21 to +25	—	—	54	13.5	4	2.0	41	10.25
+26 to +30	—	—	23	5.7	—	—	27	6.75
+31 to +35	—	—	17	4.25	—	—	22	5.5
+36 to +40	—	—	5	1.25	—	—	8	2.0
+41 to +45	—	—	3	0.75	—	—	6	1.5
+46 to +50	—	—	—	—	—	—	2	0.5

Electrocardiographic Findings.—Since the x-ray and radioscopic examinations showed that many of the subjects who lived in high altitudes had a predominance of the right side of the heart, it was considered desirable to undertake an electrocardiographic study in a group of them for the purpose of obtaining further information. Electrocardiograms were obtained in 100 subjects between the ages of 24 and 58 years. In each subject the three classic leads, six unipolar precordial leads, and three unipolar limb leads were made. For the unipolar leads the central terminal of Wilson, with Goldberger's[17] modification, was used. The electrocardiograms were taken after a rest of ten minutes.

The most essential measurements of the different deflections and time intervals were made, and a three-dimensional study related the results, especially, to the electrocardiographic patterns of right ventricular hypertrophy described by Goldberger,[18] Sodi Pallares,[19] and Myers and Stofer.[20] A more complete study with a larger number of subjects is now being made. In the present series the most important results were as follows:

Rate: Monge[21] has demonstrated by clinical examination that inhabitants of high altitudes often have a slow cardiac rate which may not exceed 35 and 40 beats per minute. In the subjects of our series the recorded beats were between 45 and 84, with an average rate of 66.5 beats per minute.

P Wave: The P wave did not show any important abnormality of duration or amplitude. This wave was often slurred, particularly when the tracings were characteristic of cor pulmonale.

P-R Interval: This interval was within normal limits in relation to the heart rate. The average duration was 0.165 second.

The QRS Complex: The mean manifest axis was determined following the axial system of Sodi, Cuellar, and Cabrera.[22] The QRS complex was found to be markedly deviated toward the right (between +90 and +180 degrees) in 59 per cent of the tracings and strongly deviated toward the left (between −90 and −180 degrees) in 21 per cent of the tracings. In the remaining subjects it was found between −10 and +90 degrees. The size of the R and S waves in the classic leads, expressed in millimeters, are given in Table II.

TABLE II.

DEFLECTION	AVERAGE (MM.)	EXTREMES OF AMPLITUDE (MM.)
R_1	3.35	1.00– 8.50
R_2	6.00	1.00–15.20
R_3	5.60	1.00–18.50
S_1	4.59	0.50–12.00
S_2	4.65	0.00–12.10
S_3	2.10	0.00– 8.10

Comparing the maximum and the minimum values with those given by Kossman and Johnston,[23] it can be observed that, as a general rule, R tends to be small and S larger in the first and second derivations, while the opposite occurs in the third derivation. The ventricular complex was classified as being of the S type when this deflection was larger than R in the corresponding lead. In 30 per cent of the series the QRS complexes were of the S_1 type; in 32 per cent, of the S_1 and S_2 type; and in 34 per cent, of the S_1, S_2, and S_3 type. In the precordial leads a positive R (larger than S) was found in V_1 in 30 per cent of the subjects, and in V_1 and V_2 in 6 per cent. The S deflection was larger than R in all the precordial leads when deviation of the axis toward the right or the left was quite accentuated. This configuration was seen particularly in tracings in which the main deflection was negative in the three classic leads. The time of intraventricular conduction was within normal limits in 72 per cent of the cases, the average duration being 0.085 second. In 21 per cent it was between 0.11 and 0.12 second and in seven subjects whose tracings showed the characteristics of right bundle branch block, QRS had a value between 0.12 and 0.14 second.

T Wave: The T wave was inverted or diphasic in Lead III in 55 per cent of the electrocardiograms and in Leads II and III in only four subjects. In the precordial leads, T was negative or diphasic in V_1 in forty-eight subjects; in V_1 and V_2 in eighteen subjects; in V_1, V_2, and V_3 in ten; and in V_1, V_2, V_3, and V_4 in two subjects.

Q-T Interval: The length of this interval was found to be within the normal limits assigned by Ashman and Hull[24] in all instances. Electrocardiographic signs of right branch block were observed in 7 per cent of the tracings, and 23

per cent of the records showed the characteristic aspect of right ventricular hypertrophy (cor pulmonale). In twenty-seven individuals the tracings suggested right predominance, even though they did not fulfill the requirements pointed out by Goldberger, by Sodi, and by Myers. It is interesting to note that x-ray examinations were more useful in discovering right ventricular hypertrophy than were electrocardiograms.

Heart Sounds.—In the natives or residents of high altitudes three or even four heart sounds are often heard. These are diagnosed clinically as reduplications of the first and second cardiac sounds. Phonocardiographic study has demonstrated that in most instances these reduplications are real; that is, they are due to the separation of the sound components. The reduplications of the second sound are found associated mainly with radiographic or electrocardiographic signs of predominance of the right side of the heart. The third cardiac sound was often recorded.

Principal Physiologic Aspects of Circulation.—In a group of sixteen subjects selected for their age, ability to cooperate, and prolonged residence at high altitude, the following determinations were made: (1) output per minute; (2) stroke volume; (3) cardiac index; (4) arterial tension; (5) venous pressure; and (6) arm-tongue circulation time (decholin) and arm-lung time (ether). The results were compared with the results of the same determinations made in a group of subjects who lived at sea level. These results have been summarized in Table III.

TABLE III. MAIN CIRCULATORY CHARACTERISTICS DETERMINED IN SIXTEEN NORMAL NATIVE SUBJECTS LIVING AT AN ALTITUDE OF 4,540 METERS, AND IN TWENTY NORMAL NATIVE SUBJECTS LIVING AT SEA LEVEL (LIMA)

	LIMA (SEA LEVEL)			MOROCOCHA (4,540 METERS ALTITUDE)		
	AVERAGE ± E. P.		EXTREME VALUES	AVERAGE ± E. P.		EXTREME VALUES
Cardiac output per minute (L./min.)	3.77	0.04	3.29 –4.36	3.81	0.03	3.35 –4.15
Stroke volume (c.c. per contraction)	61.0	1.29	49.0 –85.0	63.0	1.19	52.0 –77.0
Cardiac index (L./M_2 of body surface)	2.23	0.02	1.95 –2.45	2.42	0.03	3.35 –4.15
Systolic arterial pressure (mm. Hg)	121.0	1.69	109–140	116	1.70	108–126
Diastolic arterial pressure (mm. Hg)	72.3	0.86	60– 85	73	1.00	59 –83
Venous pressure (cm. H_2O)	8.4	0.33	6.7 –14.5	9.9	0.24	7.5 –15.5
Arm-tongue circulation time (sec.)	13.4	0.20	10.0 –17.5	16.5	0.55	11.0 –32.0
Arm-lung circulation time (sec.)	5.8	0.22	4.2 –9.0	7.6	0.18	6.0 –10.0

The most important deviations that can be observed in Table III are the following: The systolic arterial pressure tends to low values, as has been proved by Miranda[25] in an extensive series of determinations. The diastolic arterial pressure is within normal limits, so that there is a slight decrease of the pulse pressure. The venous pressure is above the limits obtained at sea level with the same methods and by the same observer. The arm-tongue and arm-lung circulation time are slightly prolonged. The cardiac output and stroke volume, respectively, expressed as liters per minute and cubic centimeters per contraction, are within normal limits, but if these data are referred to body surface a slight increase is found. The cardiac output, however, has been determined with the acetylene method of Grollman[26] and we have good reason to think that the application of the method, even though corrections be made, is not to be recommended.

DISCUSSION

From these results, it may be concluded that the heart of a man living at high altitudes (4,540 meters) presents a certain degree of globular enlargement, with a predominance of the right side in a good number of cases, as is shown by the x-ray films and electrocardiograms. Since studies of animals living at the same altitude have shown that the cardiac enlargement is due to myocardial hypertrophy,[6] it is logical to admit that, in man, hypertrophy may be the determining cause of the increased cardiac dimensions. According to the work of Wearn and associates[27-29] and of Roberts,[30,31] every hypertrophied heart has an imperfect intrinsic circulation in proportion to its degree of hypertrophy. In the long run, therefore, hypertrophy becomes harmful to the organism. There is nothing at present which demonstrates that the heart at high altitudes does not follow this rule. As to the cause of the hypertrophy, it might be considered a consequence of the "anoxia anoxica" which determines all physiologic changes dependent on altitude. The predominance of the right side which is found in many cases must be related to the pulmonary congestion and other pulmonary modifications which were studied by Hurtado.[32] The moderate increase of the venous pressure and the prolongation of the circulation time strengthens the hypothesis of overwork of the right side of the heart. In some subjects this predominance is more evident than in others. While it has not been proved, it is probable that this may be due to a deficiency in the respiratory apparatus more than to alterations of the heart.

SUMMARY AND CONCLUSIONS

Measurements of cardiac size have been verified and a study has been made of some aspects of the circulatory physiology in subjects who are natives living at 4,540 meters above sea level. The determinations include the following: The study of 400 frontal x-ray films in which the transverse diameter and the frontal area of the cardiac silhouette were measured, using the method of Ungerleider and Gubner; eighty fluoroscopic examinations of the heart, especially in the anterior oblique position; analysis of 100 electrocardiograms obtained in the

three classic leads, six unipolar precordial leads, and three unipolar limb leads; and, finally, the study in sixteen subjects of the cardiac output per minute, the stroke volume, the arterial pressure, the venous pressure, and the arm-tongue and arm-lung circulation time.

The anlysis of the data obtained gives the following general results:

1. An increase in the transverse diameter of the heart in 69.5 per cent of the cases with an average increase of 19.5 per cent. An increase of the frontal area of the cardiac silhouette in 67 per cent of the subjects with an average increase of more than 21.3 per cent was found.

2. In 65 per cent of eighty fluoroscopic examinations of individuals who showed an increase of their cardiac measurements, clear signs of right heart predominance were found.

3. The electrocardiograms showed the following interesting findings: A_{QRS} was deviated toward the right, between +90 and +180 degrees, in 59 per cent of the subjects; A_{QRS} was strongly deviated toward the left, between −90 and −180 degrees, in 21 per cent. S was larger than R in all, or in almost all, precordial leads in subjects in whom a high degree of deviation of the axis to one side or to the other existed. The principal deflection was negative in Lead I in 30 per cent of the subjects, negative in Leads I and II in 32 per cent, and negative in the three classic leads in 24 per cent. The intraventricular conduction time was found increased in 28 per cent of the subjects, including seven with right bundle branch block. Tracings typical of cor pulmonale were often observed.

4. Phonocardiographic study demonstrated that the reduplications of the cardiac sounds which have been frequently found in the natives living in high altitudes were reduplications in the strict sense. The reduplications of the first sound accompanied bradycardia, and those of the second sound were associated with radiographic or electrocardiographic manifestations of right predominance.

5. Among the principal circulatory characteristics studied, the most important findings were the following: A slightly high cardiac index; low systolic arterial pressure; normal diastolic arterial pressure, with a decreased pulse pressure; venous pressure higher than that at sea level; and slightly delayed arm-tongue and arm-lung circulation times.

6. All these data suggest that the heart of a native, or of an individual who has lived for a long time at a high altitude, hypertrophies by the effect of "anoxia anoxica." The predominance of the right side, which is found frequently, is due to overwork of this portion of the heart which is the result of functional and anatomic alterations of the lung. At high altitudes the heart is working close to its maximum capacity. A very long stay in high altitudes, therefore, is harmful from a cardiocirculatory point of view.

REFERENCES

1. (a) Hurtado, A.: Am. J. Physiol. **100**:487, 1932.
   (b) Hurtado, A.: J.A.M.A. **120**:1278, 1942.
2. Aste-Salazar, H., and Hurtado, A.: Am. J. Physiol. **142**:733, 1944.
3. Hurtado, A., Merino, C., and Delgado, E.: Arch. Int. Med. **75**:284, 1945.
4. Aste-Salazar, H.: Data not published.
5. Strohl, J.: Zool. Jahrb. **30**:1, 1910.
6. Van Liere, E. J.: Am. J. Physiol. **116**:290, 1936.
7. Rotta, A.: Rev. argent. de cardiol. **10**:186, 1943.
8. Campbell, J. A.: Brit. J. Exper. Path. **16**:39, 1935.
9. Kaufman, H., and Meyer, H. H.: Med. Klin. **44**:45, 1917.
10. Meyer, H. H.: J. de med. de Bruxelles **17**:409, 1912.
11. Rotta, A.: An. Fac. de cien. méd. Asunción **21**:285, 1938.
12. Miranda, A., and Rotta, A.: An. Fac. de cien. méd. Asunción **27**:50, 1944.
13. Kerwin, A. J.: Am. Heart J. **28**:69, 1944.
14. Ungerleider, H. E., and Clark, C. P.: Am. Heart J. **17**:92, 1939.
15. Ungerleider, H. E., and Gubner, R.: Am. Heart J. **24**:494, 1942.
16. Schwedel, J. B.: Clinical Roentgenology of the Heart. Annals of Roentgenology Series, 18, New York, 1946, Harper & Brothers.
17. Goldberger, E.: Am. Heart J. **23**:483, 1942.
18. Goldberger, E.: J. Lab. & Clin. Med. **30**:213, 1945.
19. Sodi Pallares, D.: New Bases of Electrocardiography, Mexico, 1945, Institute Nacional Cardiología, p. 70.
20. Myers, G. B., and Stofer, B. E.: J. Lab. & Clin. Med. **31**:493, 1946.
21. Monge, C.: (a) An. Fac. de cien. méd. Asunción **17**:1, 1935.
   (b) Science **95**:79, 1942.
22. Sodi, P. D., Cuellar, P., and Cabrera, C. E.: Arch. Inst. cardiol. México **14**:142, 1945.
23. Kossman, C. E., and Johnston, F. D.: Am. Heart J. **10**:925, 1935.
24. Ashman, R., and Hull, E.: Essentials of Electrocardiography for the Student and Practitioner of Medicine, ed. 2, New York, 1941, The Macmillan Co.
25. Miranda: Data not published.
26. Grollman, A.: The Cardiac Output of Man in Health and Disease, Springfield, Ill., 1932, Charles C. Thomas, Publisher.
27. Shipley, R. A., Shipley, L. J., and Wearn, J. T.: J. Exper. Med. **65**:29, 1937.
28. Roberts, J. T., and Wearn, J. T.: Am. Heart J. **21**:617, 1941.
29. Wearn, J. T.: Bull. Johns Hopkins Hosp. **68**:363, 1941.
30. Roberts, J. T.: Texas State J. Med. **38**:221, 1942.
31. Roberts, J. T.: M. Ann. District of Columbia **14**:483, 1945.
32. Hurtado, H.: Aspectos Fisiologicos Patólógicos de la Altura, Ed. Rimac, Lima, 1943, p. 4.

STUDIES ON FLUTTER AND FIBRILLATION

II. The Influence of Artificial Obstacles on Experimental Auricular Flutter

A. Rosenblueth and J. Garcia Ramos
Mexico, D. F., Mexico

THE circus-movement theory of auricular flutter postulates that in this type of cardiac activity there are one or more impulses which are propagated in one direction around a determined closed path and which recur cyclically and regularly. In the first paper of this series, Wiener and Rosenblueth (1946) showed that for this type of propagation one or more obstacles are necessary, surrounded by conducting tissue. The obstacle should have an effective perimeter sufficiently long to contain the wave represented by the impulse, in order that the front of this wave may always find nonrefractory tissue ahead.

According to the theory, the cyclic frequency of flutter depends on two factors: the conduction velocity of the impulses in the auricular muscle and the effective perimeter of the obstacle around which the impulses circulate. We mean here by "effective perimeter" the length of a string tightly surrounding the single or multiple obstacle. This perimeter is adequate if its length is greater than the product of the conduction velocity of the impulses times the duration of the functional refractory period.

Lewis and collaborators attempted to obtain direct evidence in favor of the circus-movement theory as follows. Lewis, Drury, and Iliescu (1921) showed that in patients with auricular flutter the electrical axis of the P wave rotates 360 degrees during each cycle. Lewis, Feil, and Stroud (1920) studied the long-lasting episodes of experimental flutter which are occasionally seen in dogs after rapid electrical stimulation of the auricle. On the basis of latency measurements, they concluded that this flutter is due to circus-movement of impulses around the orifices of one or both venae cavae or, more exceptionally, around one of the auriculoventricular orifices.

In the present study a more direct test of the theory was attempted by investigating what influence reversible (cocaine) or irreversible (mechanical injury) blocks applied to different regions of the auricle exert on the ease of production of auricular flutter and on its rate.

From the Department of Physiology and Pharmacology of the National Institute of Cardiology of Mexico.
Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

METHOD

In dogs anesthetized with dial (0.5 to 0.55 c.c. per kilogram of body weight intraperitoneally), under artificial respiration, the heart was exposed by removal of a portion of the sternum and some of the costal cartilages. In some instances the thoracic sympathetic chains were excised from the stellate to the fourth or fifth ganglion; a later section of the vagi in the neck severed all the nervous connections of the heart.

Two or more pairs of electrodes were fixed on the auricles for stimulation or recording. These electrodes were light steel spring forceps clamped to the auricular wall. The tension on the spring was enough to hold the clamps in place and not strong enough to cause any important damage to the wall. The electrodes were attached to light, flexible, insulated copper wires, which were supported so that they could follow freely the movements of the heart, and did not give rise to recording artifacts of mechanical origin.

The cardiac impulses were amplified through five push-pull stages coupled by capacities and resistances. They were then led to a cathode ray oscillograph where they could be observed or photographed. The electrical stimuli were condenser discharges with frequency controlled by a thyratron; the shocks were sometimes rendered diphasic by means of a transformer. The amplitude of the stimuli was adjusted to two to five times the threshold.

The reversible blocks were obtained by local applications of cotton wicks moistened with a 2.5 to 5 per cent solution of cocaine hydrochloride. Irreversible blocks were produced by crushing the muscle with a dissecting forceps. The injuries could be identified and measured at the end of the experiments by the local extravasation of blood; they did not lead to tearings of the wall.

RESULTS

1. *Criterion Adopted to Determine the Existence of Flutter.*—If flutter is defined in terms of the circus-movement theory of its mechanism, as stated in the introduction, it is clear that it is not possible to affirm its occurrence on the basis of records from one pair of electrodes. The existence of this type of activity can be inferred only from such records. In the description of the experimental results the term flutter will be employed to denote the appearance of impulses with the following characteristics: (1) their pattern differs from that of the normal beats, thus indicating that they were not originated at the pacemaker; (2) their frequency is greater than that of the beats of the pacemaker but does not exceed the limit imposed by the refractory period of auricular muscle when uninfluenced by vagal activity, that is, 8 per second; (3) their rate is slightly accelerated by vagal stimulation or by injection of adrenaline which has an important decelerating or accelerating influence on the rate of the heartbeats; (4) they are rhythmical and their pattern is invariable or recurs with regular cycles. As will be shown in the discussion, these characteristics warrant the inference that this activity corresponds to flutter, as defined by the circus-movement theory.

2. *Flutter in the Normal Auricle.*—In denervated, uninjured auricles only rarely may flutter activity be elicited with the characteristics described. Our observations agree with those of Lewis, Feil, and Stroud (1920). Intense and rapid stimulation of any auricular region for a sufficiently prolonged period usually leads to atypical activity, which outlasts the period of stimulation for some seconds and which is then followed by normal beats (Fig. 1). These after effects of the stimuli, however, do not exhibit the features adopted here to define flutter: the impulses are irregular, arrhythmic, and rapid. This type of auricular response to electric stimulation will be described in more detail and discussed in a subsequent paper.

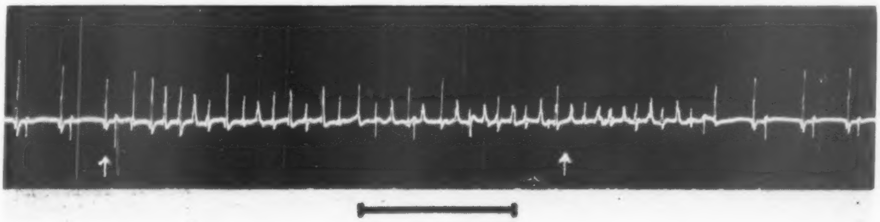


Fig. 1.—Short-lasting series of irregular, relatively fast, impulses that illustrates the typical after-effects of a brief period of strong and rapid stimulation of a normal dog's auricle. Electrical record from two leads on the right appendix. Between the two arrows stimuli were applied at the rate of 50 per second to another pair of electrodes near the superior vena cava. Time calibration, one second.

In exceptional cases, on the other hand, periods of stimulation similar to those described may be followed by relatively slow (6 to 8 per second), regular impulses with all the characteristics of flutter. In their study of experimental auricular flutter, Lewis, Feil, and Stroud used occasional instances of this sort.

The rate of this flutter is in accord with the hypothesis that the effective central obstacle around which the impulses circulate is constituted by the orifices of the two venae cavae. The effective perimeter of these two orifices is approximately 8 centimeters. The conduction velocity of the dog's auricle varies between 40 and 110 cm. per second, according to Lewis, Drury, and Bulger (1921). The theoretic conduction velocity, calculated from the rate of the flutter and the measured perimeter of the assumed obstacle, is from 55 to 65 cm. per second. The theoretic values and the experimental measurements are thus in satisfactory agreement.

If the inference is accepted that the cavae may provide the dual obstacle around which travel the impulses of the experimental flutter in normal auricles, the fact that flutter appears infrequently challenges an explanation. The study of Wiener and Rosenblueth (1946) suggests that the infrequency of occurrence is due to the difficulty of initiating one-way flutter waves around the dual obstacle. Even though a one-way impulse may meet one of the cavae end-on, and thus propagate unidirectionally around it, the presence of a bridge of conducting tissue between the two vessels will usually lead to two-way conduction around the second cava, with a cancellation of the two wave fronts.

This argument led us to expect that a block of the conduction of impulses through the intercaval auricular bridge would ensure the ready and regular appearance of experimental flutter. This expectation was confirmed experimentally.

3. *The Appearance of Flutter After Injuries to the Intervenous Bridge.*—In the eleven dogs studied for this purpose, flutter could be readily elicited after the crushing of the intervenous conducting bridge converted the two cavae into a single obstacle. One or a few periods of intense and rapid stimulation were adequate for the purpose. The rate of the flutter was approximately the same as that measured in the exceptional instances previously cited.

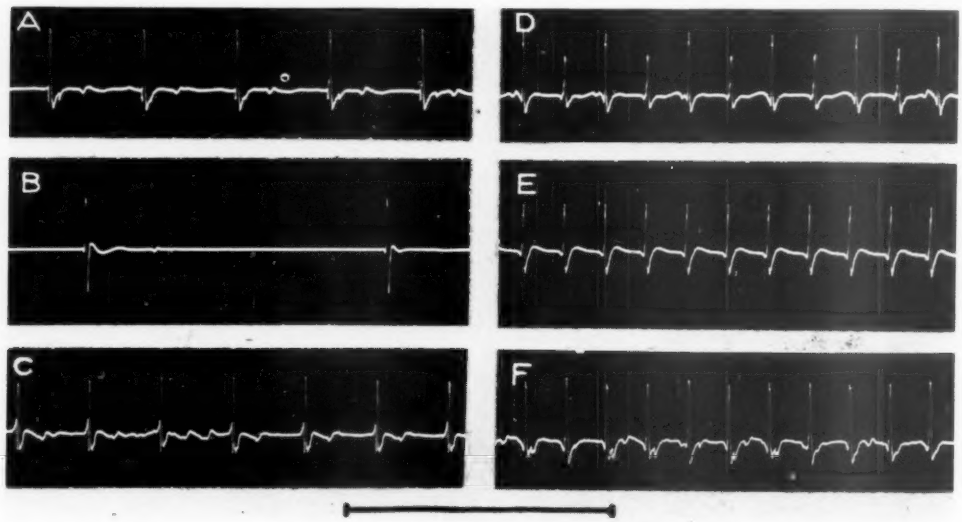


Fig. 2.—Characteristics of the enduring flutter obtained from a brief period of electrical stimulation, after the auricle has been crushed between the two cavae. Recording electrodes placed in front of the superior vena cava. Time calibration, one second.

A, *B*, and *C*, Controls before the flutter was elicited. *A*, Normal beats; *B*, effects of stimulating the right vagus with a frequency of 12 per second; *C*, thirty seconds after an injection of adrenaline (20γ).

D, *E*, and *F*, Flutter. *D*, Alternation of the flutter impulses; *E*, effects of vagal stimulation as in *B*; *F*, effects of an injection of adrenaline as in *C*.

The rhythmicity and regularity of the flutter impulses is illustrated in Fig. 2, *D*. Strong stimulation of the right vagus, which slowed the heart beats considerably (Fig. 2, *B*), slightly accelerated the flutter and eliminated the alternation of responses which had prevailed before the stimulation (Fig. 2, *E* and *D*). An injection of adrenaline in a dose sufficient to cause significant acceleration of the beats (Fig. 2, *C*) modified only slightly the rate of the flutter (Fig. 2, *F*).

Not only was it easy to initiate enduring flutter episodes after injury to the intervenous region, but it was also quite simple to interrupt a given episode at any time by the application of a few additional electrical stimuli to any region in the auricle. A technique that was effective consistently was the following.

The stimuli were applied with a frequency slower than that corresponding to the flutter. The frequency was then gradually increased until it became slightly higher than that of the flutter. At this stage the stimuli soon gained control of the auricular activity; that is, the oscillograph showed that each stimulus was followed by a response with a fixed latency. If the intensity or the rate of the stimuli was then decreased, it was found that the heart was beating normally.

In some animals, after the initial injury to the intervenous region, a progressive series of additional injuries was made, starting at the lower edge of the orifice of the inferior vena cava and extending the limit of the obstacle toward the auriculoventricular groove. As long as there was a conducting bridge between the obstacle and the ventricle (that is, as long as the obstacle was surrounded by intact auricular tissue), the flutter persisted or could be initiated, but as soon as the injury reached the boundary of the auricle (that is, as soon as the obstacle was no longer entirely surrounded by conducting tissue), the flutter disappeared and could no longer be reinitiated. These observations confirm the inference that the central obstacle for the cyclic propagation of the flutter waves was, in fact, constituted by the orifices of the two cavae.

4. *Reversible Blocks of the Intervenous Region.*—In order to convert the two orifices of the cavae into a single obstacle, it is not indispensable to damage irreversibly the intervenous conducting bridge; a reversible block at this region should be sufficient to permit the initiation of flutter. While ethyl chloride and ether were found ineffective, local applications of a 2.5 to 5 per cent solution of cocaine gave rise, in the majority of the cases tested, to a reversible block adequate for the purpose. The experiment was successful in relatively small dogs (those weighing less than 10 kilograms), while it sometimes failed in larger animals, probably because the external application of the anesthetic does not lead to a block of all the muscular elements at the treated region when the muscular wall is thick.

A typical observation will be described. Strong and rapid stimuli were repeatedly applied through a pair of electrodes attached near the superior cava. The records obtained through another pair of electrodes placed near the inferior cava showed that these stimuli had as aftereffects only the short-lasting, rapid, irregular activity illustrated in Fig. 1 but failed to elicit enduring flutter. A cotton pledget soaked with the cocaine solution was applied for about one minute to the intervenous bridge and was removed. Repetition of the stimulation now gave rise to typical flutter activity, which lasted for one or two minutes. Further renewal of the stimuli failed to evoke flutter unless the intervenous region was again treated with cocaine. Several episodes of flutter could thus be provoked in a given animal by repeated applications of the blocking agent. Unlike the flutter obtained after irreversible mechanical injury, these episodes lasted for only relatively short periods of time and disappeared spontaneously. It is clear that a total block of conduction at the intervenous bridge is a necessary condition not only for the initiation, but also for the endurance of the propagation of flutter waves around the two cavae, when the block is caused by cocaine.

In some animals, after several reversible cocaine blocks had been made and several flutter episodes recorded, the intervenous region was crushed and a new period of long-lasting flutter was initiated and recorded. The rate in all these different episodes of flutter was the same, thus showing that the central obstacle was the same in all cases.

5. *The Influence of the Perimeter of the Artificial Obstacles Upon the Frequency of Flutter.*—In order to test this influence the following observations were carried out. An injury was made at the intervenous region (Fig. 3, *1*). Flutter was elicited by appropriate stimulation and its rate was measured. A second

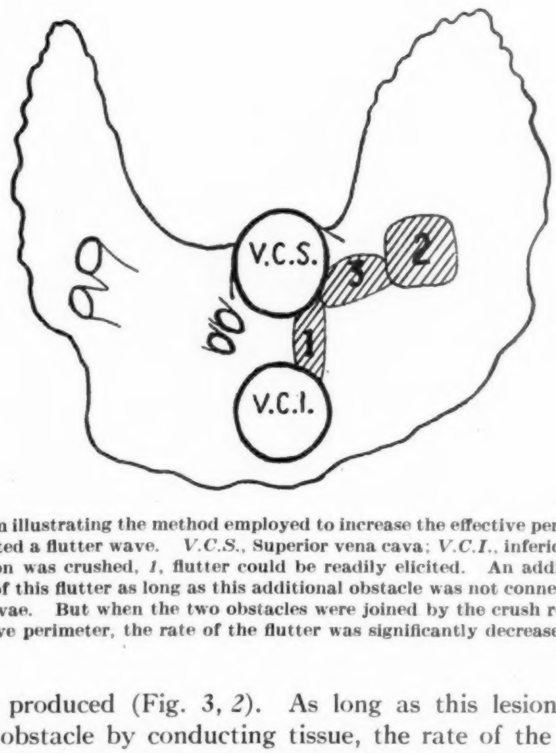


Fig. 3.—Diagram illustrating the method employed to increase the effective perimeter of an obstacle around which circulated a flutter wave. *V.C.S.*, Superior vena cava; *V.C.I.*, inferior vena cava. When the intervenous region was crushed, *1*, flutter could be readily elicited. An additional injury, *2*, did not modify the rate of this flutter as long as this additional obstacle was not connected with that represented by the two cavae. But when the two obstacles were joined by the crush represented in *3*, thus increasing the effective perimeter, the rate of the flutter was significantly decreased.

lesion was then produced (Fig. 3, *2*). As long as this lesion was separated from the initial obstacle by conducting tissue, the rate of the flutter was not modified, but as soon as it was connected to that initial obstacle (Fig. 3, *3*), the rate of the flutter became significantly slower. Thus, in a typical case, the rate of the flutter after the intervenous region had been crushed was 7.1 per second in several episodes. After the obstacle had been enlarged by the additional injuries, the rate dropped to 6.3 per second. At the end of the experiment the obstacles were measured. The effective perimeter of the first obstacle (the two cavae) was 9.0 cm. and that of the second obstacle (the cavae plus the additional injuries) was 12.7 centimeters. The conduction velocities of the flutter waves, calculated on the basis of the corresponding rates and perimeters, are, respectively, 64 and 80 cm. per second. These theoretical values are in agreement with the experimental measurements of Lewis, Drury, and Bulger which have been

referred to. The fact that the conduction velocity was less when the obstacle was smaller is in accord with the observations of these authors, and our own, that the propagation velocity decreases when the conducting tissue is in the relatively refractory period; that is, as the obstacle decreases in size, the gap between the front and the rear of the flutter wave becomes smaller—the tissue ahead of the front is relatively more refractory.

DISCUSSION

That the activity described here as flutter is due to a circus movement of impulses around an obstacle, or, in other words, that the circus-movement theory of flutter is appropriate, is supported by the following considerations.

1. The regularity of the impulses recorded shows that they reached the recording electrodes through a fixed path. The cases where alternation of responses was present do not vitiate this argument, for it is applicable to every other impulse. Alternation is probably due to the refractoriness of some of the recording elements at the time of arrival of the impulses which gives rise to the smaller electrical deflections.

2. In many animals having an appropriate intervenous lesion, the diphasic records of the impulses in different episodes of flutter, although constant in frequency, could exhibit a reversal of polarity; that is, while in some of the episodes one of the recording electrodes could be first negative and then positive, in other episodes the same electrode could become first positive and then negative with respect to the other lead. The constancy of the frequency is in agreement with the assumption of an obstacle with a constant perimeter; the reversal of polarity is reasonably explained by the assumption that the impulses went around this obstacle in some cases in one direction and in others in the opposite direction.

3. The slight acceleration of the flutter impulses which usually ensued upon stimulation of the vagus reveals a fundamental difference between the normal beats and flutter. The vagus slows the automatic beats of the cardiac nodal tissues. There is no reason, however, for it to slow flutter, since the impulses recorded during this activity are not due to automatic discharges from any region of the heart but are due to the continuously recurring propagation of one or more impulses. Lewis, Drury, and Bulger (1921) have shown that the vagus decreases the refractory period of auricular muscle and that it may increase its conduction rate when this velocity is subnormal because the propagation occurs through relatively refractory tissue. In unpublished observations we have confirmed the data and inferences of Lewis and collaborators. The acceleration of flutter consequent to vagal stimulation is thus readily explained.

4. The slight acceleration of flutter which is obtained by stimulation of the cardiac branches of the sympathetic system or by injections of adrenaline reveals in turn the different nature of flutter as compared to normal beats and can be explained also by an indirect effect on the conduction velocity of auricular muscle via the duration of its refractory period. We have found

(unpublished observations) that adrenaline and sympathin, like acetylcholine, shorten the refractory period.

5. The satisfactory accord between the conduction velocity calculated from the measurements of the rate of flutter and of the effective perimeter of the assumed obstacles and the conduction velocity determined experimentally is direct evidence in favor of the circus-movement theory.

6. Finally, as another datum in direct support of the theory may be adduced the fact that enduring flutter can be initiated only if the assumed obstacle is entirely surrounded by conducting tissue. This datum excludes the possibility of spontaneous beats of ectopic origin.

The preparation described (Result 3) is of obvious importance for the study of flutter. Up to now this study has been handicapped by the rarety of occurrence of long-lasting flutter in normal auricles. Following the simple technique which we have described, flutter episodes may always be readily initiated; they will usually persist indefinitely and can thus be observed at length; they can be extinguished at will, if necessary for the purposes of the experiment.

SUMMARY

In denervated normal dog's auricles, enduring activity with the characteristics of flutter, as defined by the circus-movement theory, can be elicited only rarely by electrical stimuli. If the conduction of impulses through the auricular fibers which lie between the orifices of the two venae cavae is blocked reversibly (cocaine) or irreversibly (crushing), however, activity of this type may be readily evoked and may last as long as the block persists. The importance of this simple preparation for the study of flutter is emphasized.

The activity in question is not initiated at the pacemaker. It is rhythmic and regular (Fig. 2, *D*). Its rate is greater than that of the normal beats (Fig. 2, *D*). This rate is slightly accelerated by vagal stimulations (Fig. 2, *E*) and by injections of adrenaline (Fig. 2, *F*) that have an important typical influence on the rate of the heartbeats (Fig. 2, *B* and *C*). These features are reasonably explained by the circus-movement theory of flutter. In agreement with the theory, additional injuries to the auricle that increase the effective perimeter of the obstacle constituted by the two cavae (Fig. 3) proportionately decrease the rate of flutter. Also in harmony with the theory is the fact that flutter can be obtained only if the obstacle is entirely surrounded by conducting tissue.

REFERENCES

1. Lewis, T., Drury, A. N., and Bulger, H. A.: Observations Upon Flutter and Fibrillation. Part VI. The Refractory Period and Rate of Propagation in the Auricle: Their Relation to Block in the Auricular Walls and to Flutter, etc., Heart **8**:83, 1921.
2. Lewis, T., Drury, A. N., and Iliescu, C. C.: A Demonstration of Circus Movement in Clinical Flutter of the Auricles, Heart **8**:341, 1921.
3. Lewis, T., Feil, H. S., and Stroud, W. D.: Observations Upon Flutter and Fibrillation. Part II. The Nature of Auricular Flutter, Heart **7**:191, 1920.
4. Wiener, N., and Rosenblueth, A.: The Mathematical Formulation of the Problem of Conduction of Impulses in a Network of Connected Excitable Elements, Specifically in Cardiac Muscle, Arch. Inst. cardiol. México **16**:205, 1946.

SYNCHRONIZATION OF AURICULAR AND VENTRICULAR BEATS DURING COMPLETE HEART BLOCK

M. SEGERS, J. LEQUIME, AND H. DENOLIN
BRUSSELS, BELGIUM

IN AN experimental work, one of us has shown that, if two isolated frog hearts are placed in contact, there may occur a synchronization of their rhythm (Segers[5]); however, this phenomenon only occurs when the two hearts beat at almost the same rhythm. This proves that interreactions may be developed between neighboring tissues, even when no anatomic connections can be traced between them. It has been shown that such interreactions result from both anatomic and mechanical excitations which are exerted by each of the two hearts on the other.

The existence of interreactions between distinct cellular elements placed in contact with each other is a well-known fact in regard to the nervous tissue. Jasper and Monnier[3] have shown, for example, that an excitation can be transmitted from one neurone to another by simple contact. Phenomena of interneuronic synchronization have also been observed during rhythmic activity of peripheral nerves and in the central nervous system. In view of these facts, we had wondered whether similar interreactions might not occur between auricles and ventricles in patients presenting complete A-V heart block. We were able to register such a phenomenon in the case which follows.

REPORT OF CASE

V. H., a 77-year-old man, was admitted to the hospital on Jan. 15, 1944. For six months he had been troubled by attacks of dizziness and unconsciousness, especially after exertion. On examination, the pulse was slow, with a rate of about 36 beats per minute. There was an occasional accentuation of the first sound. The roentgenogram showed an increase of all the diameters of the heart. Blood pressure was 220/120.

Electrocardiographic Findings.—Electrocardiograms were recorded daily with the patient at bed rest; they revealed an auriculoventricular block of a very peculiar type. The average duration of the P-P intervals was 0.85 second and that of the R-R intervals exactly twice as long, 1.70 seconds. These intervals changed spontaneously within limits that reached 10 per cent of their average duration. This fluctuation was independent of breathing, and irregular, but the auricular and ventricular rhythms always remained in a 2:1 ratio (Fig. 1). There

From the Department of Medicine and Solvay Institute of Physiology, University of Brussels.
Preliminary communication read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

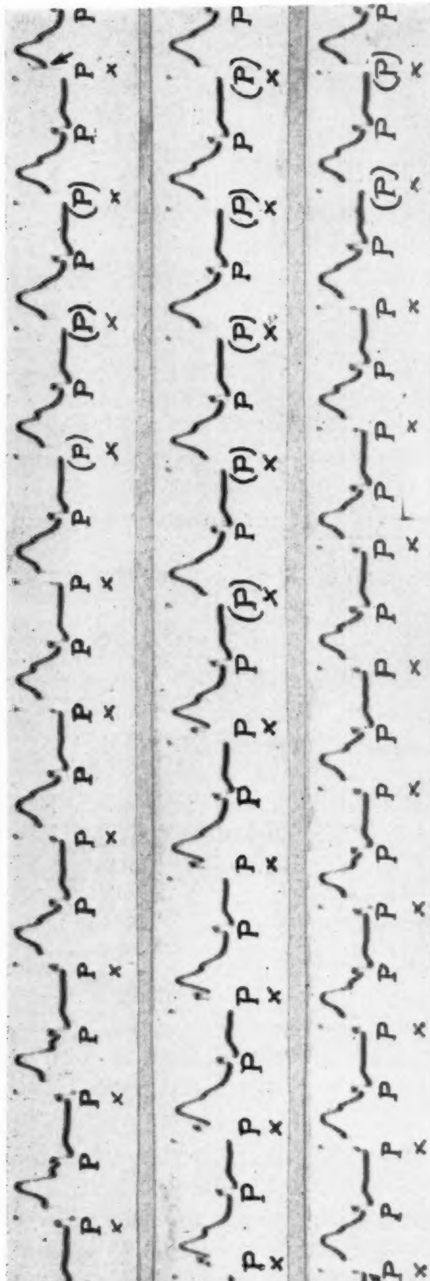


Fig. 1.—Record of complete block with A-V synchronization. Continuous tracing taken with the patient at bed rest (Lead IV R). Every other P wave, marked by a cross, remains in the close neighborhood of R; the 2:1 auriculoventricular synchronization is obvious.

was indeed a close correlation between the activities of the two pacemakers of the heart: in every other auricular cycle, the P wave occurred systematically a little before or a little after the R wave. The respective positions of these two waves were not always the same: according to fluctuations of the rhythm, there was a constant wandering of the P position with respect to R, but the duration of the P-R or R-P interval never exceeded 0.18 second (Figs. 1 and 2). This connection was not fortuitous, for it was recorded daily in this patient, while he was at bed rest, in continuous tracings showing several hundred beats.

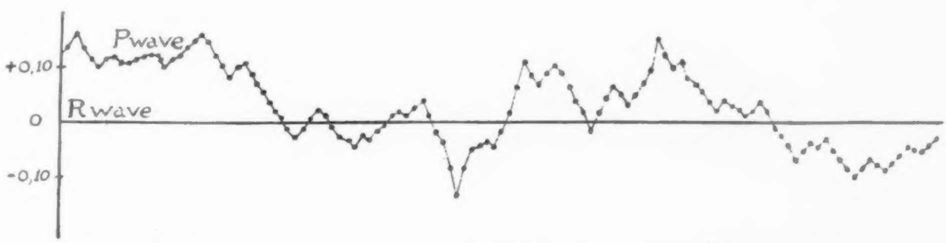


Fig. 2.—Positions of P with respect to R during 121 successive ventricular beats (patient at rest). There is a constant wandering of the position of the P wave with respect to R, but the P-R or R-P interval never exceeds 0.18 second.

The electrocardiograms had two characteristics. Whatever the duration of the recording, the auricular beats were always twice as numerous as the ventricular beats. Although there were slight fluctuations of the rhythm, every other P wave continued to be situated in close proximity to an R wave. However, this was not an incomplete dissociation of a 2:1 type, since the P wave continuously changed its position with respect to the R wave.

An exercise test produced an acceleration only of the auricular rhythm. With the increase in the auricular rate the synchronism of the two pacemakers disappeared (Fig. 4): but a few minutes after the exercise, the auricular rhythm slowed to its former rate and the 2:1 synchronism reappeared. The fact that the auricular frequency could change without influencing either the rhythm or the form of the ventricular complexes shows that complete heart block existed.

Either the 2:1 auriculoventricular synchronism was merely fortuitous, or it was the result of neighborhood interreactions developing between the two pacemakers. The first hypothesis cannot be accepted, for several facts cannot be explained by chance alone. For instance, the fluctuations of the auricular and ventricular rhythms were not absolutely identical, but they did present a correlation, as is proved by the following numerical facts. The duration of two successive P-P intervals varied from 1.53 to 1.84 seconds; the R-R intervals varied from 1.54 to 1.80 seconds. If the two rhythms were independent, there could have been at times a difference of as much as 0.30 second in the duration of the simultaneous P-P-P and R-R intervals; this difference, however, never exceeded 0.10 second. In a more general way, if we measure systematically the difference between the simultaneous P-P-P and R-R intervals, we find a greater number of small values than could be attributed to chance alone (Fig. 3). This correla-

tion between the fluctuations of the two rhythms cannot be attributed to a common vagosympathetic control, since an exercise test produced an acceleration of the auricular rhythm only.

If the auriculoventricular synchronism was merely fortuitous, the P waves could have occupied any position relative to R; the fact is that the P-R or R-P intervals never became longer than 0.18 second at rest. This gives another proof of the correlation between the activities of the auricles and ventricles.

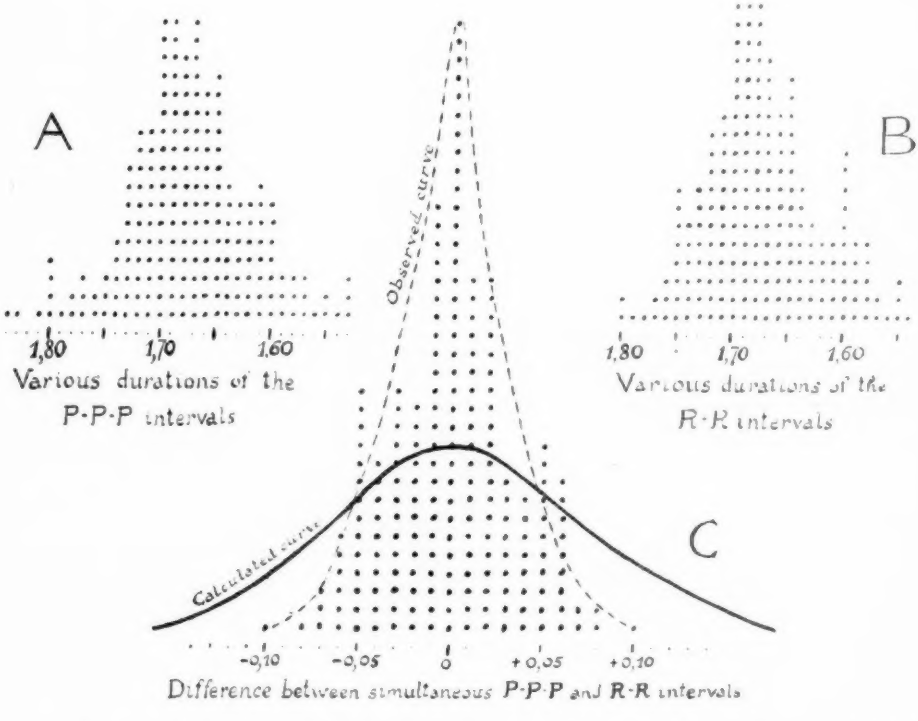


Fig. 3.—Statistical study of the fluctuations of the rhythm observed during 200 successive beats. In *A*, *B*, and *C* the number of dots indicates the number of times each interval was observed. *A* and *B* show the frequency of appearance of the several P-P-P and R-R intervals. *C* concerns the differences in duration between the simultaneous P-P-P and R-R intervals; the observed curve indicates how often the various differences have been noted. The calculated curve shows how often these differences would appear if they were merely fortuitous; the curve is calculated according to the probabilities of combinations between the numerical data of *A* and *B*. The number of small values is clearly higher than the calculated one, which implies the existence of a correlation between the fluctuations of the P-P-P and R-R intervals.

As has been stated, after exercise the auricular rhythm was accelerated without a measurable increase of the ventricular rate; but even after exercise, the two pacemakers were not always completely independent. When the increase in the auricular rate was not very much, the P waves did not constantly change their position with respect to the R waves. They did alter their relationship to R rapidly, from beat to beat, when the P waves were relatively far from

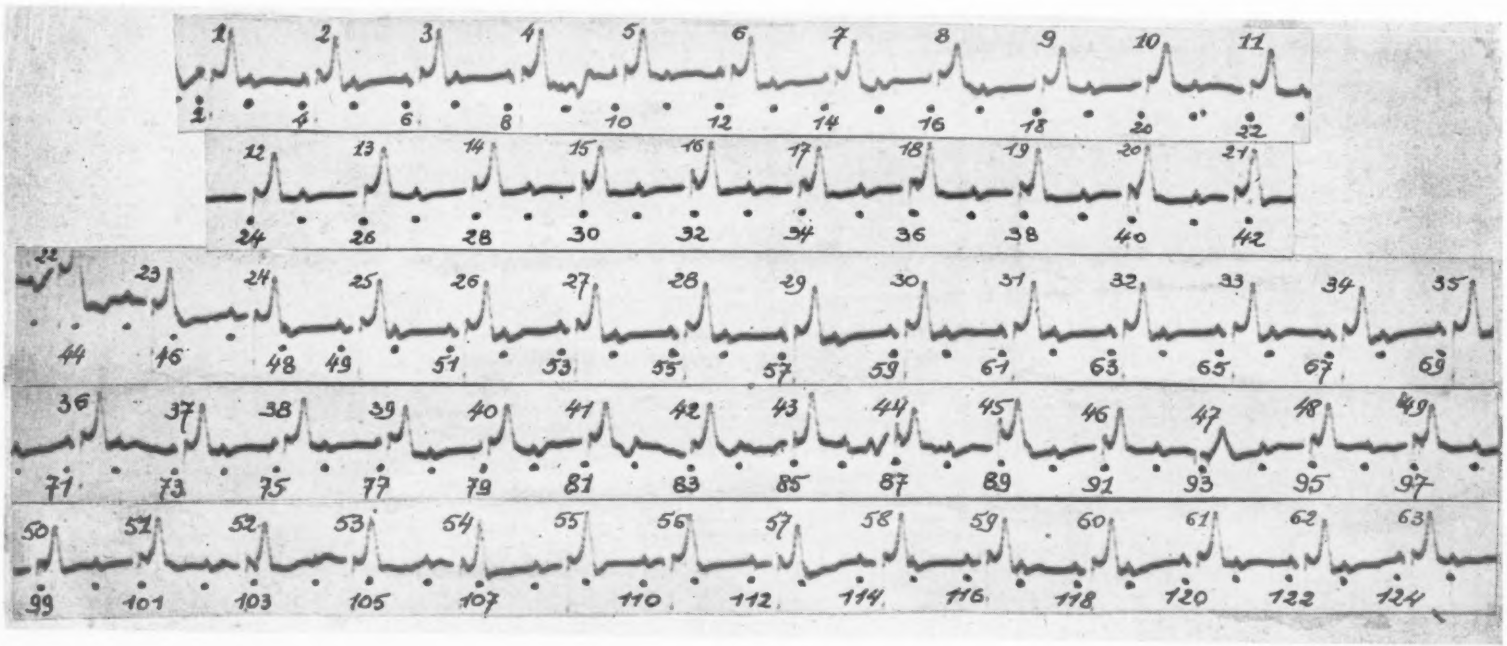


Fig. 4.—Complete block showing the close and dependent association of P and R waves (phénomène d'accrochage). Continuous tracing taken after light exertion. The dots mark the position of the P waves; the auricular and ventricular beats are numbered. The auricular waves indicated by an even number are "hooked" to the R wave during the first twenty ventricular beats. After a rapid change, the P waves marked with an uneven number assume the close association with R waves during the ventricular beats twenty-five to fifty. Then the same sequence of events takes place all over again.

the R waves, but they moved from the R waves slowly when the P-R or R-P intervals were small (Figs. 4 and 5). In other words, whenever the interval between the P and R waves was a small one, these waves had a tendency to remain closely associated or "hooked" together. This phenomenon undoubtedly proves the presence of interreactions between ventricles and auricles which tends to synchronize their rhythms.

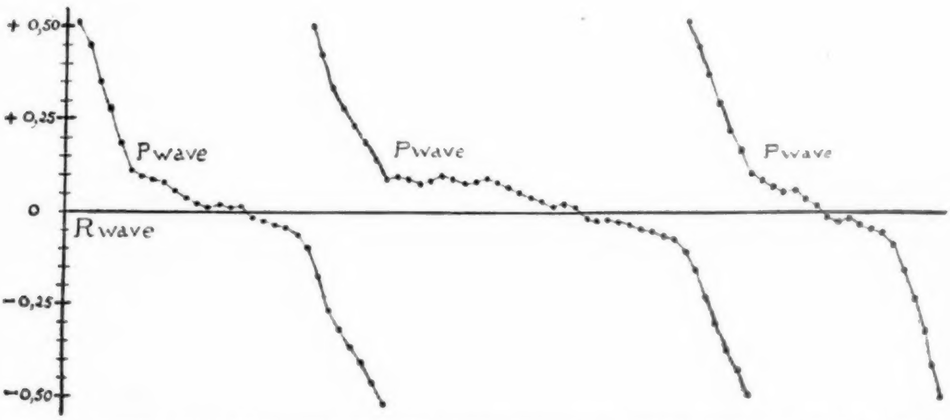


Fig. 5.—Position of P with respect to R during eighty successive ventricular beats (after light exertion). The wandering of P becomes slower in the neighborhood of R.

DISCUSSION

The synchronization of auricular and ventricular rhythms during complete heart block is not a very frequent phenomenon, but when it occurs, it is not due merely to chance. That there exist neighborhood interreactions between auricles and ventricles is shown by the following facts:

1. The auriculoventricular synchronism remains constant even when there are fluctuations of the rate amounting to as much as 10 per cent of the average rate.
2. The P waves remain always in close association with the R waves.
3. Even when the synchronism is abolished by exercise, periodically the P and R waves may assume a close and apparently dependent association (phénomène d'accrochage).

The neighborhood interreactions responsible for the synchronization probably result from both mechanical and electrical excitation exerted by the ventricles on the auricles. But the relation so created is by no means as reliable as that normally assured by the bundle of His; indeed, slight exercise is sufficient to destroy the synchronization of the two pacemakers.

Several authors[2,4,6] have stated that, during complete heart block, the rhythms of the two pacemakers can remain synchronized in a 1:1, 2:1, or 3:1 ratio. The case we have reported demonstrates this fact.

The condition described by French authors as "isorhythmic dissociation" seems to be explained by a similar phenomenon. Of course, in the isorhythmic dissociation, the conduction in the bundle of His is generally not altered, but there exists an autonomous and synchronous activity of auricles and ventricles. This autonomy of the two pacemakers results from the mutual "extinction" of the normal and retrograde impulses in the bundle of His;[1] such a peculiar state can be maintained as long as the two pacemakers beat at the same rhythm. If our interpretation of the isorhythmic dissociation is accepted, the block of the bundle of His should thus not be a necessary condition for the appearance of a synchronization between two distinct pacemakers in the heart.

SUMMARY

During complete heart block, the auricular and ventricular rhythms may in some cases remain synchronized in a 2:1 ratio during very long periods. After exercise, the synchronization disappears, but a close association of a P wave and an R wave (phénomène d'accrochage) may occur. These facts must be attributed to neighborhood interreactions developing between ventricles and auricles, without any conduction pathway. They are similar to the synchronization which is observed when two frog hearts are placed in contact.

We therefore conclude that the rhythms of auricles and ventricles are not necessarily independent during complete heart block.

REFERENCES

1. Dressler, W.: Dissoziationen und Interferenzen bei partiellem Herzblock, Ztschr. f. klin. Med. **111**:23, 1929.
2. Fischer, R.: Ueber das Vorkommen einfacher zahlenmässiger Beziehungen zwischen der Frequenz dissoziiert schlagender Herzabschnitte, Ztschr. f. klin. Med. **116**:466, 1931.
3. Jasper, H., and Monnier, A. M.: Transmission of Excitation Between Excised Non-Myelinated Nerves. An Artificial Synapse, J. Cell. & Comp. Physiol. **11**:259, 1938.
4. Kisch, B.: Beobachtungen bei einem Kranken mit totalem Block, Cardiologia **2**:47, 1938.
5. Segers, M.: Les phenomenes de synchronisation au niveau du coeur, Arch. internat. de Physiol. **54**:87, 1946.
6. Van Buchem, F. S. P.: Dissoziation zwischen Atrium und Ventrikel. Erklärung des partiellen Herzblocks, Ztschr. f. klin. Med. **110**:401, 1929.

COMPARATIVE STUDY OF BLOOD CULTURES MADE FROM ARTERY, VEIN, AND BONE MARROW IN PATIENTS WITH SUBACUTE BACTERIAL ENDOCARDITIS

M. Salazar Mallén, M.D., E. Lozano Hube, Q.B.P., and Mario Brenes, M.D.
Mexico, D. F., Mexico

BLOOD cultures are of great value in patients with subacute bacterial endocarditis, first, because of their diagnostic importance and, second, because they provide knowledge about the bateriologic characteristics of the causative organism. In the case of penicillin-sensitive bacteria, this knowledge permits a determination of the sensitivity of the organism to the drug as a preliminary step to prescribing adequate dosage. Disregard of this may lead to undertreatment or to waste of valuable therapeutic material, since the proper dose in cases of *Streptococcus viridans* infection may vary from 100,000 units in infections with relatively sensitive strains to several million units per day in less sensitive strains, such as *Streptococcus fecalis*.

It has been suggested in recent years that arterial blood has a higher bacterial content in patients with septicemia. Murray and Moosnick[1] conducted a comparative study of blood cultures made from the femoral artery and the antecubital vein. In twenty-seven patients studied, fifteen yielded positive cultures: nine of the cultures were positive in the arterial blood only; one was positive in the venous blood only; and five were positive in both arterial and venous blood. Beeson, Brannon, and Warren[3] found only a very slight difference between the bacterial content of blood from the antecubital vein and the femoral artery; the hepatic and renal veins, however, were notable for their low bacterial content. The only study made with venous and bone marrow blood is that of Barbagallo,[4] who found a higher proportion of positive cultures in the latter. In a recent study of patients with brucellosis, the authors[5] obtained results comparable with those of Barbagallo, the marrow being positive in some instances, when peripheral blood was sterile. This finding prompted us to conduct a similar study in cases of subacute bacterial endocarditis to obtain information about the relative value of venous, arterial, and marrow cultures.

The clinical material consisted of eighty-eight patients, seen at this Institute during the years 1945 and 1946. A set of three cultures (vein, artery, and bone marrow) was taken from the patient as soon as ordered, regardless of the presence or absence of fever. In all, 109 "sets of three" cultures (327 cultures in all) were taken from the eighty-eight patients, several individuals having cultures made more than once.

From the Laboratory of Bacteriology and Immunology, National Institute of Cardiology.
Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.

The sites for puncture were disinfected with tincture of iodine, ether, and alcohol, and the operator always used sterile rubber gloves. The punctures were made in the antecubital vein, the radial artery, and in the sternal bone at the level of the second intercostal space. In the latter case, to avoid discomfort to the patient, the skin and the periosteal tissues were infiltrated with 2 per cent novocain.

Blood was collected in vials containing enough dried sodium citrate to inhibit blood coagulation. The bone marrow was immediately inoculated into a broth tube, in the ratio of 2 drops per 5 c.c. of media. With citrated blood, poured plates were prepared with melted nutrient agar in the ratio of 1 c.c. of blood to 10 c.c. of media. The remaining blood (5 c.c.) was inoculated in a flask containing 100 c.c. of nutrient broth. None of the media contained clarase or other penicillin inhibitors. All the cultures were incubated aerobically at 37° C. The liquid media cultures were examined microscopically after seventy-two hours and, if found negative, were again examined after seven and ten days. Cultures were considered positive when growth in the liquid cultures was observed which yielded characteristic colonies when planted on solid media. The poured plates were examined after twenty-four, forty-eight, and seventy-two hours, and one week.

Of the 109 "sets of three" cultures (327 cultures in all) referred to previously, only twenty-four (from seventeen patients) gave positive results from one or more of the three sources (artery, vein, and bone marrow). The data are recorded in Table I.

TABLE I. CULTURES OF VENOUS AND ARTERIAL BLOOD AND BONE MARROW FROM PATIENTS WITH SUBACUTE BACTERIAL ENDOCARDITIS (POSITIVE RESULTS)

CASE	ARTERIAL BLOOD	VENOUS BLOOD	BONE MARROW	PENICILLIN TREATMENT
1 (H. I.)	–	–	+	Yes
2 (H. I.)	+	+	–	No
3 (D. M.)	–	–	+	Yes
4 (D. M.)	+	+	–	No
5 (A. C. H.)	–	+	+	Yes
6 (A. C.)	–	+	+	No
7 (A. C. P.)	+	+	+	No
8 (A. A.)	–	–	+	Yes
9 (L. E.)	+	+	+	Yes
10 (L. E.)	–	+	–	Yes
11 (V. C.)	+	+	+	Yes
12 (V. C.)	+	+	+	Yes
13 (V. C.)	+	+	+	Yes
14 (I. L.)	–	–	+	Yes
15 (A. S. A.)	+	+	+	No
16 (E. M.)	–	–	+	No
17 (E. M. N.)	–	+	+	No
18 (M. A.)	+	+	+	No
19 (M. A.)	+	+	+	No
20 (M. A.)	+	+	+	No
21 (S. L.)	+	+	+	No
22 (A. E.)	+	+	+	No
23 (J. S.)	+	+	+	No
24 (L. M. A.)	+	+	+	No

The comparative study of the three different types of culture is shown in the same Table I. Positive results were obtained from arterial blood in fifteen cultures, from venous blood in nineteen cultures, and from bone marrow in twenty-one cultures. *Streptococcus viridans* was the organism isolated in all the cultures. Venous blood was positive in four instances in which arterial blood was negative. In all instances in which arterial blood was positive, venous blood was also positive. In three patients in whom the cultures from bone marrow were negative, positive cultures were obtained from both artery and vein in two patients, and from the vein alone in one patient. Of the five patients whose venous blood was negative, and the bone marrow positive, four were under penicillin treatment.

There was no significant difference in the relative number of colonies observed in poured plates which contained, respectively, arterial and venous blood. The total of the colony countings per milliliter of blood in poured plates containing arterial blood was 541 as compared with 523 in plates containing venous blood (Table II).

TABLE II. NUMBER OF COLONIES FOUND IN POURED PLATES MADE WITH VENOUS AND ARTERIAL BLOOD FROM PATIENTS WITH SUBACUTE BACTERIAL ENDOCARDITIS

CASE	ARTERIAL BLOOD	VENOUS BLOOD
1 (H. I.)	0	0
2 (H. I.)	8	0
3 (D. M.)	0	0
4 (D. M.)	0	0
5 (A. C. H.)	0	22
6 (A. C.)	0	6
7 (A. C. P.)	0	0
8 (A. A.)	0	0
9 (L. E.)	13	7
10 (L. E.)	0	7
11 (V. C.)	20	15
12 (V. C.)	12	14
13 (V. C.)	24	19
14 (I. L.)	0	0
15 (A. S. A.)	17	9
16 (E. M.)	0	0
17 (E. M. N.)	0	0
18 (M. A.)	0	0
19 (M. A.)	0	0
20 (M. A.)	0	0
21 (S. L.)	40	29
22 (A. E.)	209	131
23 (J. S.)	8	39
24 (L. M. A.)	190	225
Total	541	523

SUMMARY

1. A set of three cultures (arterial, venous, and bone marrow) was taken 109 times (a total of 327 cultures) from eighty-eight patients with subacute bacterial endocarditis. Of the 109 sets of cultures, twenty-four were positive in one or more of the three cultures.

2. The incidence of positive cultures was highest in cultures made from bone marrow inoculated into nutrient broth (twenty-one of the twenty-four patients). The incidence was slightly lower in cultures containing venous blood (nineteen of the twenty-four patients). The incidence was lowest in arterial blood cultures (fifteen of the twenty-four patients).

3. Judging from the mean colony counts in poured plates containing arterial and venous blood, there was no obvious advantage of one method over the other.

4. Bone marrow cultures were positive in four of five patients under penicillin treatment.

5. The data emphasize the usefulness of bone marrow cultures in the diagnosis of subacute bacterial endocarditis. It is to be noted, however, that in some instances bone marrow culture was negative when arterial or venous blood cultures were positive.

REFERENCES

1. Murray, M., and Moosnick, F.: J. Lab. & Clin. Med. **26**:382, 1940.
2. Touroff, A. S. W.: Proc. Soc. Exper. Biol. & Med. **49**:568, 1942.
3. Beeson, P. B., Brannon, E. S., and Warren, J. V.: J. Exper. Med. **81**:9, 1945.
4. Barbagallo, G.: Policlinico (sez. med.) **45**:230, 1938.
5. Brenes, M., Salazar Mallén, M., and Lozano, H. Elena.: Rev. Med. d. Hosp. Gen. **7**:89, 1944.

Summaries of Other Communications Presented at the Second Inter-American Congress of Cardiology

A number of papers which are presented in abstract form in this issue will be published in full in future issues of the American Heart Journal.

THE DIAGNOSTIC VALUE OF ELECTROCARDIOGRAPHIC PATTERNS BASED ON AN ASSAY OF 261 ADDITIONAL AUTOPSIED CASES

L. N. Katz, M.D., D. Feldman, M.D., and R. Langendorf, M.D.
Michael Reese Hospital, Chicago, Ill.

In order to determine the accuracy and dependability of our criteria of electrocardiographic diagnosis, a critical analytic study was made on a series of patients with autopsy control. The necropsy files for a period of five years (May, 1940, to May, 1945) were examined and those cases who had come to necropsy within two months after having an electrocardiogram were selected for study. Two hundred sixty-one consecutive cases were thus studied. The electrocardiograms on each patient were interpreted without consulting the anatomic data, and then the interpretations correlated with the necropsy findings. The accuracy of our interpretations was assayed, and all cases in which a discrepancy existed between the electrocardiographic diagnosis and the necropsy data were studied in detail. Thirteen specific electrocardiographic patterns were separated, as well as nonspecific electrocardiographic abnormalities, and normal records. Forty-one (15.7 per cent) of our cases constituted discrepancies, the remaining 220 (84.3 per cent) showing agreement between the electrocardiographic findings and the pathologic data.

In general, the electrocardiogram was found to be a good index of anatomic normality and abnormality of the heart, although its use is limited by its inability in many cases to distinguish clinical from subclinical forms of heart disease. Occasionally, a normal electrocardiogram may be found with anatomic heart disease, and therefore a normal electrocardiogram cannot be considered to rule out heart disease. A definitely abnormal electrocardiogram, on the other hand, is excellent evidence for anatomic abnormality of the heart.

Ventricular hypertrophy is usually reflected in the electrocardiogram by patterns of heart strain. However, ventricular hypertrophy may, on occasion, be present without electrocardiographic evidence of heart strain, and conversely, other changes may mimic the pattern of heart strain. For example, left heart strain may be imitated by an old anterior wall infarction. With the use of multiple chest leads, left ventricular hypertrophy more often gives rise to a characteristic strain pattern than does right ventricular hypertrophy. With combined ventricular hypertrophy the patterns of the predominantly hypertrophic ventricle are seen more often than a pattern diagnostic of combined heart strain.

Recent myocardial infarctions of any variety, especially if serial records are available, are seldom missed electrocardiographically, although old infarctations or severe coronary arteriosclerosis without confluent infarctation may give rise to patterns indistinguishable from recent infarctions, presumably because of coronary insufficiency. Old, healed myocardial infarctions can often be diagnosed electrocardiographically but not with the regularity of recent infarctions. Often a healed infarction leaves as its only electrocardiographic residue nonspecific abnormalities. As with recent infarctions, old infarction patterns may be mimicked by other conditions. Coronary arteriosclerosis without confluent infarctions generally resulted in nonspecific electrocardiographic abnormalities.

The patterns described for congenital heart disease were diagnostic in this series, although the pattern of Katz and Wachtel may be mimicked on occasion in the adult by other conditions. The patterns of uremia, of acute diffuse pericarditis with or without concomitant myocardial infarction, and of acute and chronic cor pulmonale were all diagnostic when encountered, but the electrocardiographic pattern is not invariably present in these conditions. A pattern similar to a recent posterior wall infarction may be seen in acute cor pulmonale.

Mitral P wave was in this series diagnostic of severe rheumatic mitral disease, and P pulmonale was in every case associated with either chronic cor pulmonale or chronic pulmonary pathology (emphysema in all cases), except in one case of congenital heart disease in which it accompanied right auricular involvement. Anatomic chronic cor pulmonale may exist in the absence of a P pulmonale.

A variety of miscellaneous cardiac abnormalities gave rise to nonspecific electrocardiographic changes.

The results in this study definitely indicate that the recognition of specific electrocardiographic patterns greatly enhances the diagnostic usefulness of the electrocardiogram.

CHRONIC HEART INVOLVEMENT IN CHAGAS' DISEASE

Luis V. Decourt, M.D., Jose Ramos, Jr., M.D., Bernardino Tranchesi, M.D.,
Ignacio A. Corea, M.D., J. Cavalheiro Dias, M.D.,
and Gaspar Tisi, M.D., Delegate Members
University of Sao Paulo, Brazil

The authors point out that an increasing interest in Chagas' disease has led to the recognition of a considerable number of cases that have cardiac involvement. Complement fixation tests, done routinely in a general hospital, show a 4 per cent incidence. This suggests that many cases formerly diagnosed chronic myocarditis might have been more properly diagnosed "trypanosome involvement of the heart." Of the twelve cases studied, ten of the patients lived in shacks where triatomideos (bedbugs) which are known vectors, were found. In all patients the disease began insiduously and presented the picture of a chronic illness; in none was the picture that of an acute illness. The authors consider that profound weakness is the most striking symptom. Syncope was commonly encountered and occasionally gave the first clue to the diagnosis. In some instances this symptom was undoubtedly due to complete auriculoventricular dissociation. Palpitation was noted as well as bradycardia and weak pulse. All patients had congestive heart failure. Not uncommonly the congestive failure was progressive and ended in sudden death. Of six patients who died, only one had symptoms for four years, the others had had sypmtoms for less than one year. One of these had been ill but one month and died suddenly after treatment with digitalis.

Teleroentgenograms showed dilatation of the heart in all cases. Pulsations of the heart were of small amplitude. Electrocardiograms frequently revealed changes in conduction. In two instances auriculoventricular block was present. Various degrees of intraventricular block were present. In two instances there was definite right bundle branch block. This latter finding has been reported by others and is considered one of the peculiarities of the disease.

Histologic changes consisted of degeneration of the myocardial fibers due to multiplication of the parasites within the heart muscle, with focal or diffuse inflammatory reactions near the vessels. Isolated nests of parasites were noted and in three cases were found deep between muscle fibers. The authors noted diffuse edema of a degree sufficient to "dissociate the walls of vessels."

COMPARATIVE STUDY OF DIFFERENT PRECORDIAL LEADS

JORGE MENESES HOYOS, M.D., OFFICIAL DELEGATE, AND A. GONZALEZ TOMAYO, M.D., CENTRAL MILITARY HOSPITAL OF MEXICO, MEXICO

1. Each kind of precordial lead (from CR_1 to CR_6, from CL_1 to CL_6, from CF_1 to CF_6, from V_1 to V_6) was recorded in ten normal controls. A comparison was then made of the findings in precordial leads recorded by using Wilson's central terminal (Leads V_1 to V_6) and the ordinary types of precordial leads (CR_1 to CR_6, CL_1 to CL_6 CF_1 to CF_6) in about one hundred patients with heart disease. These were selected to include the following conditions: left or right axis deviation, ventricular hypertrophy, angina pectoris, coronary sclerosis, and myocardial infarction.

2. The different precordial leads recorded in normal persons with the precordial electrode in the same place were very much alike; there was no important change when the indifferent electrode was moved from the right arm to the left arm, to the left leg, or united to the Wilson's terminal. There were significant variations with the changes in the position of the precordial electrode, but the findings recorded at Positions 1 through 6 were very similar in the CR, CL, CF, and V leads. As the electrode was moved from right to left (from Position 1 to Positions 5 or 6) R gradually increased and S decreased. A downward or negative T was not found normally in precordial leads, except in those taken with the precordial electrode at the right margin of the sternum. A downward or negative P was often found in Leads CF_1 to CF_3 or CF_4.

3. In cases of ventricular hypertrophy a wider QRS complex in precordial leads and a positive shift of the S-T segment in tracings made at Positions 1 to 4 was found both in leads using the Wilson terminal and in the CR leads. The R wave was of higher amplitude in Leads V_5 or CR_5 in patients with left ventricular preponderance and in Leads V_1 or CR_1 in patients with right ventricular preponderance.

4. In patients with angina pectoris or with coronary sclerosis no significant change was found in precordial leads. In both V and CR leads, however, there was a slight shift of the S-T segment upward in tracings made from Positions 1 to 3, and downward in tracings taken from Positions 5 and 6.

5. A downward or negative T wave was found to be a more constant and important change in the electrocardiogram in patients with old myocardial infarction. A downward T in the third standard limb lead and an upward T in precordial leads was found in posterior myocardial infarction, using the V, the CR, or the CF leads. A downward T in precordial leads in anterior and lateral myocardial infarction was found using the V, the CR, or the CF leads. There was no important influence of the place of the distant electrode or of the terminal of Wilson in the changes in Q and R waves provoked by myocardial infarction in the patients studied.

6. Since no important variation was found in normal nor in abnormal conditions in the precordial leads using the CR or the V leads, we think there is no practical advantage in preferring the latter. CR leads are easier to be recorded. Since in some normals a downward P and a downward T was found in Leads CF_1 to CF_3, we regard CR leads as preferable.

COMPARATIVE STUDIES WITH THE THREE TYPES OF ELECTROCARDIOGRAPHIC LEADS (CLASSIC, UNIPOLAR EXTREMITY LEADS, AND MULTIPLE PRECORDIAL LEADS) IN RELATION TO CLINICAL AND RADIOLOGIC EXAMINATIONS

J. Ramos, M.D., H. K. de Melo, M.D., and S. Borges, M.D., Brazil

For the purpose of investigating which of the three types of electrocardiographic leads give better indications of changes occurring in the cardiocirculatory system, the authors studied 375 patients from the clinical, radiologic, and electrocardiographic standpoints.

The 375 patients were classified as follows: 121 showed no evidence of abnormality of the cardiocirculatory system by clinical, radiologic, and electrocardiographic study; 187 had hypertension; 23 gave a history of angina pectoris; 18 had valvular lesions; 10 had some type of congenital heart disease; and 16 patients had myocardial infarction.

Electrocardiographic studies were made with a string galvanometer. Unipolar leads of the limbs were taken with Goldberger's modification of Wilson's central terminal method.

The conclusion of the authors is that no single type of lead is to be preferred, since all three types of leads give valuable information. Precordial leads were superior to other leads in studying infarction of the anterior wall and bundle branch block. Classic and unipolar leads of the extremities gave the same results; the latter proved to be more useful because they were unipolar.

AN EASY METHOD FOR CALCULATING THE VALUE OF THE MEDIUM AXIS AND THE VENTRICULAR GRADIENT

J. Meneses Hoyos, M.D., Official Delegate, Central Military Hospital of Mexico, Mexico

1. The author proposes a very simple method for measuring the manifest mean electrical axis of QRS and the manifest ventricular gradient both in their direction and their magnitudes. The direction of the vectors can be found by means of charts like that of Dieuaide or that of Carter and Richter. But the angle *alpha* that the vectors form with the horizontal can be found also by the following formula which the author proposes:

$$\text{T angle } alpha = 1.155 \frac{e_3}{e_1} \text{ plus } 0.577$$

in which e_1 and e_3 are, respectively, the projected areas in Lead I and Lead III. With the aid of the slide rule the calculation of the direction of the desired vectors becomes an easy task.

2. The measurement of the ventricular gradient can be made by multiplying the net area of the QRST complex in Lead I by the secant of the angle *alpha* made by the vector with the horizontal.

3. The method of Ashman and the geometric procedure are described for comparison. Examples are given.

SELECTIVE PLACEMENT OF PATIENTS WITH HEART DISEASE IN COMPETITIVE EMPLOYMENT

CHARLES E. KOSSMANN, M.D., LEONARD J. GOLDWATER, M.D., AND CLARENCE E. DE LA CHAPELLA, M.D., NEW YORK UNIVERSITY COLLEGE OF MEDICINE, NEW YORK

A plan of selective placement of patients with heart disease in employment which their limited cardiac reserve will permit them to accomplish safely is presented. It requires close cooperation of the cardiac clinic with the employment service. There are three basic parts to the plan: the physical capacities appraisal of the patient, the physical demands analysis of the job, and the matching of the former against the latter when placing the patient in a job. For successful accomplishment the plan requires the participation of three specialists: the cardiologist, the job analyst, and the employment placement officer.

A special unit of the New York University Cardiac Clinic of Bellevue Hospital is utilizing such a plan in cooperation with the United States Employment Service. Known as the Work Classification Unit, it is also attempting to gather data on the effect of occupation on the course of heart diseases.

CARDIAC NEUROSIS

GABRIEL TORO VILLA, M.D., OFFICIAL DELEGATE, FACULTY OF MEDICINE OF MEDELLÍN, COLUMBIA

The cardiologist must treat in his office, not only patients having organic heart diseases, but also patients having no cardiocirculatory abnormalities. The latter constitute some 50 per cent of all persons consulting the specialist. These patients with symptoms but without organic disease can be divided into at least three groups:

1. Patients with cardiac phobia. The patient's difficulties are the result of exaggerated apprehension, of autosuggestion, or of hypochondriasis.

2. Patients with false heart disease. The physician's oversolicitous attitude or a too-thorough heart examination sometimes focuses and fixes the patient's attention upon a given symptom which in itself is of no significance. Unfortunately, the physician is sometimes responsible. All too often the improper interpretation of an unimportant auscultatory sign, the use of improper technique in taking the blood pressure, or a wrong interpretation of an electrocardiogram which is within the physiologic pattern may lead to a diagnosis of cardiovascular disease when no disease exists.

3. Patients with hyperactive cardiac reflexes who present transitory symptoms of abnormal function of the heart without organic lesion. Some of the conditions that these patients show include neurocirculatory asthenia, paroxysmal tachycardia, transitory bradycardia, hyperexcitability of the carotid sinus, and an exaggerated gastrocoronary reflex (Roemheld syndrome) caused by gaseous distention of the stomach.

To these three groups must be added those patients who develop neurosis and even psychosis as a result of arterial hypertension.

A REVIEW OF EIGHT CASES OF WOLFF-PARKINSON-WHITE SYNDROME INCLUDING FOUR CASES WITH INITIAL LEFT VENTRICULAR ACTIVATION AS DEMONSTRATED BY THE MULTIPLE PRECORDIAL LEADS

JOSEPH C. REED, M.D., ROBERT W. LANGLEY, M.D., AND
DAVID C. UTZ, M.D., LONG BEACH, CALIF.

From 6,900 patients examined by the electrocardiograph at the U. S. Naval Hospital, Long Beach, Calif., eight cases of Wolff-Parkinson-White syndrome, characterized by the short P-R interval and the wide QRS complex, were found.

The present consensus of opinion concerning the mechanism of the conduction pattern points to the presence of an anomalous muscle bundle or bundles which connect the right atrium and right ventricle, thereby providing an accessory pathway for the excitation wave. Wood, Wolferth, and Geckler have described such a pathway on the right side of the heart which was present in a patient with this syndrome. The suggestion has been made that this connection may be similar or identical to the "right lateral bundle" as described by Kent many years ago.

If the accessory muscle bundle is the mechanism for this syndrome, the patterns of the precordial leads in the present series suggest that this bundle is not restricted to the right heart. An anlysis of the precordial leads in the present eight cases indicates that in four of the patients the left ventricle was activated before the right ventricle. These four showed QRS complexes of the M shape in leads over the right side of the heart, similar to the pattern seen in right bundle branch block; the remaining four had W shaped complexes in leads from the same area, similar to that seen in left bundle branch block. In the former, it is noted that there is an initial positive deflection, which is broad at its base, in leads over the right side of the heart; and in the latter it is noted that the same initial positive deflection occurred in leads over the left side of the heart. This characteristic slurring is uncommon in cases of bundle branch block.

Three patients, two of whom were past the age of 50 years, presented definite evidence of organic heart disease. The remaining five patients revealed no apparent heart disease. Four patients had no cardiac complaints. Only two complained of palpitation or of symptoms suggesting paroxysmal tachycardia.

ALTERATIONS IN THE STRUCTURE OF THE LIVER CELL IN CONGESTIVE HEART FAILURE

ISAAC COSTERO, M.D., AND ROSARIO BARROSÓ-MOGUEL, M.D.
NATIONAL INSTITUTE OF CARDIOLOGY, MEXICO

Depolarization of the liver cell (Minkowski), which causes jaundice in hepatic cirrhosis, has a specific histologic appearance which we have called "cholechrysocytosis." It is regarded as the specific morphologic basis of "regurgitational" jaundice in hepatic cirrhosis. Its origin is explained as follows: The cells of the bile ducts have the function of regenerating those parenchymatous elements which are lost during the disease. As the process advances, the toxic substances which damage the liver cells begin to act also on the incompletely differentiated cells (metahepatocytes). In the protoplasm of these immature cells aurophile bodies appear which are characteristic of cholechrysocytosis. Jaundice follows this morphologic change. The latter represents intrinsic depolarization of the cells.

In this paper the histologic alterations of the liver in cardiac disease are summarized as follows:

1. In cardiac patients dying with chronic passive congestion of the liver, no changes of any kind were found in the cells which could be related to the intensity of jaundice. Nevertheless, great numbers of metahepatocytes, easily recognized by their tonoplasmic reticulum, were found in those patients who had developed acute degenerative changes similar in type to those found in red atrophy of the liver.

2. To explain the absence of specific cellular changes usually related to jaundice and the abundance of metahepatocytes, we assume that the liver cells destroyed during chronic passive congestion are replaced by cells of the bile ducts. But in the patient with heart disease the liver cell is not subjected to any specific toxin and thus the metahepatocytes can continue their transformation into adult parenchymatous elements without acquiring cholechrysocytosis.

3. When jaundice appears in patients with heart disease, it is due to causes other than toxemia, the most important of which is the collapse of the intratrabecular bile capillaries in the more congested sites of the hepatic parenchyma.

4. The atrophy of the liver during congestive heart failure passes through the following stages: (a) congestion of the central venules with intense anoxia and moderate compression of the liver cells; (b) hyperplasia of the reticular endothelium forming the wall of sinusoidal blood capillaries; (c) elaboration of precollagenous fibers by this hyperplastic reticular endothelium; (d) intense compression of the trabeculae through spontaneous retraction of the recently formed fibers with collapse of the intratrabecular bile capillaries and compression atrophy of the liver cells; (e) fragmentation of trabeculae into isolated cells; (f) reabsorption of the isolated atrophic cells.

5. Jaundice appears only in those patients with heart disease in whom the following two fundamental conditions are fulfilled: (a) a sufficient number of intratrabecular bile capillaries have been collapsed; (b) the great number of cells which formerly evacuated their bile through the obstructed capillaries retain their functional integrity.

6. When the secreting pole of the compressed cells has ceased to exist, the bile and the other products of cell activity are shed into the bloodstream, causing the appearance of jaundice. The process of depolarization is extrinsic in nature since the chain of phenomena which reverses the flow is not in the secreting cell but arises from the mechanical obstruction of its normal draining mechanism.

7. The multiple miliary hemorrhages, commonly found in rheumatic disease as a consequence of the changes in the wall of small blood vessels, are sometimes the cause of extrahepatic jaundice, as shown by the Van den Bergh test. This form of jaundice is completely independent of the anatomic changes present in the liver of these patients.

CARDIAC CHANGES IN MALARIAL PATIENTS

R. A. Rojas, M.D., and D. Deza, M.D., Active Members, Argentina

The authors made a careful cardiologic survey of a series of malarial patients, all of whom had positive smears for Plasmodium. The studies included clinical examinations, electrocardiograms, and radiographic examination.

Electrocardiographic and x-ray studies were made during apyrexia and before and after treatment. Abnormalities in the form and size of the heart and electrocardiographic changes noted before treatment tended to disappear in most of the cases when the disease was treated.

Anatomicopathologic studies were made in a patient who died of malaria. In the myocardium, dilatation and thrombosis of small capillaries were observed. There were no hemorrhages. Thrombi formed by masses of destroyed erythro-

cytes were present. In other places the capillary endothelium showed cytoplasmic changes with hyalinosis of the interstitial collagen tissue. Inside the thrombotic masses, as well as in the endothelial wall, numerous parasitic forms in various stages of evolution were found. Most forms belonged to the *X* erythrocytic and reticuloendothelial stages. Interstitial reactions around the capillary vessels were clearly observed near the epicardium and beyond the muscular tissue common to both ventricles. These reactions included hyalinosis of the pericapillary tissue, discrete hyperplasia of the collagen, and slight edematous infiltration. Interstitial reactions also included the formation of small nodules, consisting of histioid cells, better developed along vessels. These nodules had the characteristics of foci of reaction since young fibroblasts, small round cells, and plasma cells could be seen. Pericardial changes included some degree of edema, diffuse interstitial infiltration by histioid cells, and noticeable changes in the adjoining tissue. Lesions that are similar to the lesions described by the authors have been produced experimentally by Conejo and Libzchizt through infection with *Plasmodium gallinaceum*.

CIRCULATORY CHANGES RESULTING FROM OBSTETRIC LABOR

J. J. Sampson, M.D., Ellen Brown, M.D., and J. J. Hopper, M.D.
University of California Medical School
San Francisco, Calif.

The circulatory loads of pregnancy as determined by various workers have been summarized. The variable and undeterminable load of work of pelvic delivery is generally inconsequential but may be of such degree as to throw a considerable burden on the heart. After delivery, certain changes take place in pulse rate and blood pressure which suggest closure of an arteriovenous shunt. After delivery, effective blood volume transiently diminishes, then rises, and finally slowly returns to normal levels. The hematocrit changes indicate hemoconcentration in the immediate post-partum period. The venous pressure, while elevated for a prolonged period in patients with cardiac disease, is largely unaffected in normal individuals, except for rise following the use of pitressin or the ergot group of drugs. The dynamics of post-partum heart failure may be associated with unexplained changes in effective blood volume which could be due to transient pooling and then release of the pooled blood.

THE APEX CARDIOGRAM AND ITS UTILITY IN PHONOCARDIOGRAPHY

Ramon Aixala, M.D., Official Delegate, Cuba

In 1939, the author first pointed out the usefulness of the apex cardiogram in identifying the events of the phonocardiogram. For the purposes of this paper simultaneous records were made of the phonocardiogram and the apex cardiogram through a single cup.

The proper technique and the equipment required for making these studies is described. Typical graphic records are illustrated.

AN OBJECTIVE CLINICAL PROCEDURE FOR THE DETERMINATION OF CIRCULATION VELOCITY USING FLUORESCENT TRACER SUBSTANCES

TRAVIS WINSOR, M.D., WILLIAM ADOLPH, M.D., WALTER C. RALSTON, M.D., AND GEORGE M. LEIBY, M.D., UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES, CALIF.

The clinical applications of circulation time measurements have been limited by the inability to determine minimal circulatory retardation. Localization of altered cardiovascular dynamics likewise has been difficult using the commonly employed techniques. These obstacles can be minimized by the newer tracer methods employing longer segments of the cardiovascular system. The purpose of this paper is to (1) demonstrate the use of riboflavin as a fluorescent tracer substance, (2) present a technique which renders circulation time of greater clinical value and, (3) demonstrate the value of comparative circulation velocities in various segments of the cardiovascular system.

Fluorescent media (riboflavin and fluorescein) were injected intravenously. The time was measured to the appearance of fluorescence in histamine wheals placed on various portions of the body. Fluorescence was excited by a 100-watt filtered ultraviolet light giving maximum emission at 3,600 A°.

Arm-to-arm and arm-to-foot times were determined. The average difference between arm-to-arm times in normal subjects and in patients with congestive failure was only 18.9 seconds, whereas the average difference between arm-to-foot times in the same group was 42.3 seconds. These differences suggest that the arm-to-foot time is a more sensitive index of circulatory retardation than is the arm-to-arm time. The circulation time through a systemic arterial segment was computed by subtracting the arm-to-arm time from the arm-to-foot time. The normal average arterial circulation time was 9.5 seconds and varied between 7.5 and 11.2 seconds. Among borderline patients with subclinical congestive heart failure and in whom the arm-to-arm times were normal, the average arterial time was prolonged to 14 seconds. In clinically decompensated patients, the average arterial circulation time was 32.9 seconds and the range 14.9 to 59 seconds. The arterial circulation time did not exceed 12 seconds in normal individuals. A time greater than 12 seconds was suggestive of cardiac decompensation, even though the arm-to-arm time was within normal limits.

Mean velocities were computed for the three segments (arm-to-arm, arm-to-foot and arterial) by measuring or estimating the distance. It was found that the velocity in the arterial segment was the most sensitive index in comparing normal individuals and decompensated patients, the average difference being 7 cm. per second.

Prolonged circulation times (or decreased velocities) for the arm-to-arm and the arm-to-foot segments may be due to either right or left ventricular congestive failure or both; however, a prolonged arterial segment time may be due solely to left ventricular hypodynamic function. By the same token, a normal arterial segment time in the presence of prolonged arm-to-arm and arm-to-foot times may be due solely to right ventricular hypodynamic function. The measurement of circulatory velocities rather than circulation times is a desirable measure in estimation of altered cardiac dynamics because it eliminates the factor of distance over which blood travels in comparing the blood flow in tall and short individuals or in adults and infants. The principles involved in the localization of segmental dynamics may be applied to venous segments and to other portions of the arterial tree.

NOTE ON A PENTOSE ISOLATED FROM HEART MUSCLE

E. Sodi Pallares, D.C., F. Velez Orozco, Quim., J. M. Rivero Carballo, M.D., Active Members, National Institute of Cardiology, Mexico

It is generally believed that chemical changes in the heart muscle without accompanying histologic alteration may constitute the basis of functional disturbance.

Studies were made of the chemical constituents of the heart muscle of normal persons and of patients who died with heart failure. Drury's technique, modified by the authors, was followed. Cobra's venom was used as the hydrolytic agent. These investigations have revealed the presence in heart muscle of L-lyxose, a pentose not previously known to occur in organisms. The possible origin of this carbohydrate from alimentary mannose or galactose is pointed out.

DIFFERENT MECHANISMS OF FUSION BEATS

M. R. Malinow, M.D., and R. Langendorf, M.D., Michael Reese Hospital, Chicago, Ill.

1. A review is presented of the contributions to the understanding of the normal and abnormal spread of the cardiac impulse which have been revealed by the study of fusion beats ("transtitional complexes," "combination complexes") in the electrocardiogram.
2. A classification of fusion beats is given, based on two criteria: origin of the fusing impulses and site of fusion.
3. The various mechanisms reflected in the electrocardiogram exhibiting fusion beats are discussed and illustrated.
4. A case of Wolff-Parkinson-White syndrome with auricular fibrillation showing complexes with a transitional contour (fusion beats) is presented as new evidence to demonstrate the functioning of both the normal and an accessory pathway in the Wolff-Parkinson-White syndrome.

SIGNIFICANCE OF VENTRICULAR OXYGEN CONSUMPTION AND OF THE ENZYMATIC LIBERATION OF PHOSPHORUS IN THE MECHANISM OF DIGITALIS EFFECT

F. Guerra, M.D., Institute of Tropical Diseases, Mexico

No significant changes in the use of oxygen by the normal left ventricle "in vitro" have been demonstrated to be caused by ouabain $1:10^6$.

There is a greater phosphorus enzymatic liberation in the myosin-adenosine triphosphate system of the heart if ouabain $1:10^6$ is present. The increase is even greater if calcium is added.

The importance of the enzymatic liberation of phosphorus as an explanation of the mechanism of action of digitalis glucosides in cardiac insufficiency is emphasized.

ON WRITING SYMBOLS TO DESCRIBE CARDIOVASCULAR SOUNDS AND MURMURS WHILE LISTENING

Harold N. Segall, M.D., McGill University, Montreal, Canada

Auscultation of the heart can be practiced in at least two different manners. For one of these, this method of writing symbols to describe heart sounds and murmurs is of little or no value. For the other, it is indispensable. The observer who makes a diagnosis while listening by interpreting the total pattern of

sounds and murmurs and then writes his clinical notes in one or two brief phrases, such as "systolic murmur at apex, mitral insufficiency" or "mitral stenosis, presystolic murmur", will not be interested in using symbols for describing what he hears. On the other hand, the observer who carefully focuses his sense of hearing on each phase of the cardiac cycle, noting what he hears, needs a method to capture and hold each part of the cardiac cycle discovered as he analyses the heart sounds and murmurs. Thus, in searching the period just before the first sound for an auricular sound or murmur, and the first sound itself for duplication, then listening to the period between the first and the second sound for a mesosystolic sound or a systolic murmur, however faint, then noting the peculiarities of the second sound and, after it, searching for a third sound or a diastolic murmur, such an observer will find this method of writing symbols to describe what he hears indispensable in the practice of cardiac auscultation.

The symbols are designed to describe quantitatively the loudness and duration of each sound and murmur. For sounds, the symbols are rectangles; the vertical line (ordinate) represents loudness and the horizontal line (abscissa) represents the duration of the sound. For murmurs, waves of lines are drawn; the height represents loudness and the distance along the abscissa over which these are drawn represents the duration of the murmur. To represent high vibration frequency murmurs (blowing), the lines are drawn close together, and to represent low vibration frequency murmurs (rumbling murmurs), the lines are separated somewhat widely.

The observer writes while he is listening. This eliminates the element of memory as a source of error in describing objective signs. Bearing in mind an arbitrary standard symbol for loudness and duration of the first sound at the apex, he writes the symbols for what he hears in terms of this standard.

A full description of everything heard in a case with buttonhole mitral stenosis and aortic stenosis and insufficiency would require about 320 words, ten minutes to write them, and three minutes to read them. The record written in terms of symbols is made while the observer listens and can be read at a glance.

STUDIES ON THE HEART SOUND IN MITRAL STENOSIS

J. Meneses Hoyos, M.D., Official Delegate, R. Castaneda, M.D., and R. Mingram, M.D., Central Military Hospital of Mexico, Mexico

During the last six years more than two hundred patients with mitral stenosis were studied in the Hospital Central Militar. The studies included clinical examination, x-ray examination, laboratory studies, electrocardiograms, and phonocardiograms. In some cases necropsy examinations were made. In seven patients with mitral stenosis, phonocardiograms were recorded at many different sites across the precordium. These sites were then marked with a lead disc and recorded upon an x-ray film.

No clear difference was found between "rumbling sounds" and "murmurs." The former were lower pitched (80 to 100 vibrations per second) and occurred in the first part of diastole; the latter were higher pitched (100 to 150 and even 200 vibrations per second) and appeared toward the end of diastole (presystole). In some patients a low-pitched presystolic murmur was heard and recorded and in others an early high-pitched diastolic murmur was present. In some patients the systolic and the diastolic murmurs were found to be of the same pitch and of almost the same duration. In other patients the systolic and the diastolic murmurs merged into a "machinery" murmur. In still others the systolic and the presystolic murmurs were continuous and gave the impression of a single murmur. In many patients with mitral stenosis, proved by x-ray examination

and even by necropsy, no murmur was heard. In some patients with both mitral stenosis and insufficiency only the systolic murmur was clearly audible and recorded.

The "opening snap" was frequently recorded. The "snapping" quality of the first heart sound was often detected; in some patients it constituted the only stethoacoustic evidence of mitral stenosis. The reduplication of the second heart sound and an audible third heart sound were often heard and recorded but neither sign was characteristic.

The diastolic murmur was heard best mainly in the fourth intercostal space 4 cm. to the left of the sternal margin, but was heard often in the fifth intercostal space. Presystolic murmurs were heard best at the apex or slightly above and internal to the apex. The opening snap of the mitral valve was recorded better in the fourth intercostal space over the left border of the cardiac silhouette.

THE FIRST CARDIAC SOUND IN PREMATURE CONTRACTIONS

PEDRO COSSIO, M.D., ACTIVE MEMBER, MEDICAL FACULTY OF BUENOS AIRES, ARGENTINA

Auscultation and phonocardiographic studies in thirty instances revealed that the first cardiac sound in premature contractions is generally more intense than in preceding and subsequent normal contractions.

This increase of intensity of the sound occurs most often with auricular extrasystoles; it is less frequent with ventricular extrasystoles. In the latter, however, splitting of the sound is sometimes found and may be diagnostic.

It is suggested that the phenomenon is the result of the relaxed and dependent position of the auriculoventricular valves during the moment of production of the premature systole.

SYMPATHOMIMETIC AMINES IN THE HEART MUSCLE: THEIR PATHOGENIC AND THERAPEUTIC SIGNIFICANCE

W. RAAB, M.D., UNIVERSITY OF VERMONT, COLLEGE OF MEDICINE, BURLINGTON, VT.

Several thousand determinations of epinephrine-like compounds were carried out in blood and tissues with a modification of Shaw's colorimetric method. The results agreed well with quantitative biologic tests for sympathomimetic amines originating both in the adrenal medulla and in the entire sympathetic system (epinephrine, sympathin, and related compounds).

Increases of this material in the heart muscle of animals were found under the following conditions: electrical stimulation of the stellate ganglia and of the splanchnic nerves; injection of epinephrine and acetylcholine; physical exercise; exposure to cold temperature; thiamine deficiency. On the other hand, decreases of these compounds in the myocardium were elicited by sympathetic denervation of the heart, total sympathectomy, adrenalectomy, or combinations of these.

It was found that excessive accumulation of sympathomimetic material in the myocardium above a sharply defined critical limit is inevitably fatal in the rat through acute heart failure. Results obtained in the hearts of patients with and without cardiac disease indicate that in man the tolerance limit is somewhat lower.

Abnormally intense discharges of epinephrine-like substances into the blood during exercise were regularly observed in patients with angina pectoris on effort and, frequently, in patients with essential hypertension. In advanced

uremia the blood level of such substances is always considerably elevated and the uremic serum proved to be highly cardiotoxic.

The myocardial concentration of epinephrine-like material increases with age, reaching a maximum in the sixth decade. Abnormally high concentrations were found in hearts of patients who had died from heart failure, in one case of adrenal medullary tumor, in two cases of sudden death in young persons without morphologic pathology, and in uremic hearts.

These observations suggest a fundamental significance of the excessive accumulation of adrenosympathetic amines in the heart muscle for the pathogenesis of "degenerative" heart disease, angina pectoris, sudden cardiac death without coronary sclerosis, uremic cardiac death, and the beriberi heart.

This conception is supported by the well-known analogies between the electrocardiographic, myocardial metabolic, and structural changes produced by repeated experimental epinephrine injections and the corresponding features in "degenerative" heart disease, angina pectoris, uremia, and the beriberi heart. Furthermore, the typical occasion for angina pectoris attacks (exercise, emotion, exposure to cold) are the same which are known to elicit adrenosympathetic discharges.

The sensitization of the heart to sympathomimetic amines through the thyroid hormone, which is probably involved in the features of the thyrotoxic heart, was demonstrated by a marked lowering of the fatal myocardial threshold for epinephrine in thyroxin-treated animals.

Rational therapeutic procedures deductable from these conclusions are as follows:

1. Desensitization of the heart through elimination of the sensitizing thyroid hormone through thyroidectomy or thiouracil. The latter drug was shown to protect the heart against otherwise fatal doses of epinephrine, to diminish or abolish the effects of epinephrine injection on the normal electrocardiogram, and to free patients with angina of their symptoms for weeks or months after sufficiently long periods of treatment.

2. Pharmacologic counteraction against the effects of sympathomimetic amines. Benzyl-imidazoline and, particularly, dibenzyl-β-chloroethylamine hydrochloride, proved highly potent in protecting the hearts of animals against fatal doses of epinephrine. Their clinical usefulness remains to be studied.

3. Suppression of excessive adrenosympathetic discharges. (a) Roentgen irradiation of the adrenal glands abolished the exercise-induced abnormal sympathomimetic discharges in patients with angina and was followed by partial or complete relief for years in the majority of 150 cases. It tended to normalize the electrocardiograms of these patients partially or completely. (b) Lumbodorsal sympathectomy in patients with hypertension is often followed by a normalization of the pathologic electrocardiogram, even if the hypertension remains unchanged, probably due to a diminution of the influx of sympathomimetic amines into the heart, as is also seen in animal experiments.

It is becoming increasingly evident that some of the most common forms of heart disease which, by tradition, used to be attributed solely to hemodynamic factors, such as blood pressure, impaired coronary flow and the like, are primarily caused by biochemical processes in which the sympathomimetic amines play a dominant role.

THE CARDIAC ACTION OF CENTRAL AMERICAN SNAKE VENOM

E. GARCIA CARRILLO, M.D., ACTIVE MEMBER, COSTA RICA

The effect of snake venom on the electrocardiogram has not heretofore been thoroughly studied. The author presents his findings in eleven patients who were bitten by Central American Snakes of the genus Bothrops which are the common species in Tropical America. In a study of eight thousand autopsies, only ten deaths were attributed to the venom of *Bothrops atrox* and *Bothrops schlegelii.*

The electrocardiographic pattern in the stricken individuals was characteristic and consisted of (1) T wave of small amplitude with a rounded vertex in one or more leads, (2) slight depression of S-T in CR_5, (3) a prolonged Q-T interval. When toxic symptoms are lacking, electrocardiographic changes are absent or slight but always show the same tendency. The author suggests that the effects of snake venom on the heart could be attributed to vascular lesions, nervous influences, coronary insufficiency secondary to anemia, or to biochemical changes. He also makes the interesting suggestion that the electrocardiographic changes may be caused by changes of cellular permeability to potassium.

AN IMPROVED ELECTRIC MANOMETER FOR MEASURING THE INTRA-ARTERIAL, INTRAVENOUS, AND INTRACARDIAL PRESSURE, WITH A GENERAL THEORY OF MANOMETERS

ANDERS TYBJAERG HANSEN, M.D., AND ERIK WARBURG, M.D., THE RIGSHOSPITAL, COPENHAGEN, DENMARK

Buchtal and Warburg's condenser manometer has been redesigned by Tybjaerg Hansen with the result that the manometer in its present design yields the maximum efficiency attainable for manometers intended for blood pressure measurements by means of arterial punctures and catheterization of the heart.

The manometer is shown in Fig. 1 of the complete paper.

Due to the small, very rigid phosphor-bronze plate (thickness, 0.3 mm.; surface area, 1 cm.^{2}) forming the yielding component of the manometer, the system is very rigid, displacements being only 0.1 c.mm. at 100 mm. Hg pressure. The movements of the plate are transmitted electrically. The plate, together with a block of brass from which it is separated by a space of the width of 15 micra, forms a condenser, the capacity variations of which are caused to work in an oscillograph by means of a high frequency arrangement and a direct current amplifier.

The modulus of elasticity (E′) of the manometer is 3.3×10^9 dynes.

The compressibility of the water at this rigidity produces 40 per cent of the total change in volume (the capacity of the manometer is 2.0 c.c.).

A general theory of manometers has been evolved, the damping term having been introduced into Frank's equation of manometers.

The manometer equation of free oscillations is thus:

$$\frac{L}{\pi r^2} \quad \frac{d^2y}{dt^2} + \frac{8\,\eta\, L}{\pi r^4} \quad \frac{dy}{dt} + E'.v = 0$$

Only the modulus of elasticity, the syringe needle used (probe, catheter), and the viscocity of the liquid are decisive to the dynamic constants of the manometer.

L = Length of the needle
r = Radius of the tube
η = Viscocity of liquid in poise
v = Volume change
E′ = Modulus of elasticity of the manometer

Formulas are given for determining the natural undamped and damped frequency, as well as the degree of damping of the manometer and needle, and it is shown that a needle having a length of 5.5 cm. and a bore of 0.22 mm. gives an undamped natural frequency of approximately 60 and a damping degree of approximately 0.7, which are the appropriate magnitudes for recording pulse curves. The relation between degree of damping and amplitude is demonstrated. In the case of a probe having a length of 60 cm. and a bore of 1 mm., the undamped natural frequency is approximately 100 and the damping degree is 0.22. An extra damping should be introduced into such a system. A capillary tube of a length of 2.5 mm. with a bore of 0.1 mm. will give an undamped natural frequency of 86, the damping degree being 0.7, which is the optimum.

An easy method has been described for determining the undamped natural frequency and damping degree of the system by means of sudden and constant variations in pressure. On the basis of the formula of the transitorial part of an oscillating system, it has been shown to be convenient that the manometer has an overshoot between 5 and 10 per cent.

Pulse curves recorded by means of the manometer are demonstrated.

MEDICAL-SOCIAL FEATURES OF HEART DISEASE IN CHILE

Luis Herve, M.D., Active Member, University of Chile, Chile

The author studied the frequency, etiology, and commonest types of heart disease in Chile. The data upon which these studies were based were gathered from medical examinations made on workers, as required by the Preventive Medicine Law which is enforced in the whole country.

Heart diseases seem to be more prevalent in office workers (10.65 per cent) than in those who engage in common labor (4.38 per cent). High blood pressure, arteriosclerosis, rheumatic heart disease, and syphilitic heart disease are dominant causes of cardiovascular diseases in the entire population.

A classification of cardiovascular affections, which is based upon functional ability and is, therefore, essentially a medical-social classification, is proposed. Most patients belong to Types I and II of the classification and receive periodical clinical examination. Patients belonging to Type III are submitted periodically to preventive rest and treatment. Patients belonging to Type IV are made to retire from activities that are beyond their limited physical abilities.

The author analyzes the conditions under which preventive rest is applied and the immediate results of this benefit. Generally speaking, it can be stated that after an average period of three months' rest, 70 per cent of the patients with heart disease can resume work.

ATTACKS OF UNCONSCIOUSNESS RESULTING FROM HYPERACTIVE CAROTID SINUS REFLEX

HARRY L. SMITH, M.D., MAYO CLINIC, ROCHESTER, MINN.

A study was made of eighty-five patients with hyperactive carotid sinus reflex. Most of the patients were treated medically. Operation was performed on twenty-one patients. A brief discussion is given of the anatomy, nerve supply, and function of the carotid sinus. In the series of patients studied at the Mayo Clinic, the ratio of males to females was 5:1. The average age of the patients was 56 years. The chief symptoms were vertigo and unconsciousness; mild convulsion may be associated with the syncopal attacks. Attacks occasionally are precipitated by changing the position of the body, turning the head to the right or left, or looking upward. Any pressure on the neck, such as tight collars or carrying sacks of grain on the shoulders, also may bring on attacks. In most instances, however, the precipitating factors in the spontaneous attacks are unexplained.

The incidence and the severity of the attacks varied greatly. They varied from an occasional mild attack occurring once or twice a year to severe spells occurring many times a day.

If the symptoms are mild, no treatment is required other than reassurance. If the attacks interfere with the patient's work, he should be instructed to avoid turning his head quickly, looking upward, or stooping suddenly. He should avoid any constriction about the neck. Drugs have not been particularly satisfactory; phenobarbital has given the best results. If the attacks are severe and a thorough course of medical management has not been successful, complete denervation of the carotid sinus may be performed, but this procedure has not been entirely satisfactory.

EXPERIMENTAL AND CLINICAL STUDIES IN HYPERCHOLESTEROLEMIA AND ATHEROSCLEROSIS AND THE EFFECT OF DECHOLESTEROLIZING AGENTS

GEORGE R. HERRMANN, M.D., UNIVERSITY OF TEXAS, GALVESTON, TEXAS

It has been demonstrated that pancreatic substances and lecithins, choline, inositol, and methionine prevent and correct nutritional fatty disorders in the liver and kidney, presumably by mobilization or changing of cholesterols to more easily metabolized lecithins and lipid phosphorus. It seemed that the same decholesterolizing substances might probably effect the cholesterols in the blood plasma and possibly the cholesterols in subintimal atheromatous plaques.

In order to test this hypothesis, several control and experimental series of twenty-four 3-year-old hens of high egg-producing stock were maintained on the standard laying mash and studied. Hypercholesterolemia and high tissue cholesterol levels had been demonstrated in various control series of these old hens. In two series the additional feeding of choline chloride in 0.5 Gm. doses to twenty-six old hens of the same breed showed fairly regular reduction of cholesterol levels in the blood and in the aorta, heart muscle, and liver. The administration of inositol, 0.5 Gm. doses, to another series of 3-year-old hens had less, but still some, decholesterolizing effect. The administration of methionine in 0.5 Gm. doses per day to two other series, a total of twenty-three 2-year-old hens, had seemingly the greatest decholesterolizing effect.

In patients with hypercholesterolemia and coronary artery disease, the restriction of animal fats in the diet and the administration of potassium iodide and of thyroid extract have been shown to lower blood cholesterol levels after

six months to two years. The administration of choline, methionine, and inositol has produced, in a majority of patients, some reduction of blood cholesterol levels and slight rises in lipid phosphorus after two to six months of treatment. The basic diet is of considerable importance and in some refractory cases, the exhibition of other substances is probably necessary to accomplish decholesterolization. The enzyme system or systems responsible for the mobilization and degradation of cholesterol to lecithins are still unknown.

The present concepts of the factors concerned in the development of atheromatosis are incomplete. There has opened up at least one and possibly more new approaches to the prevention, postponement, arrest, or possibly decrease of the subintimal plaques. These plaques in secondary arteries are very often of such serious significance. Dietary restrictions of the sterol intake and the use of potassium iodide and thyroid extract judiciously in selected cases seem justified. The success of administration of the newer decholesterolizing agents seems to offer another promising method of therapeutic attack on the serious processes of premature aging.

STUDY OF CEREBRAL AND PERIPHERAL EMBOLI, REGISTERED IN THE NATIONAL INSTITUTE OF CARDIOLOGY OF MEXICO, FROM SEPTEMBER, 1944, TO MAY, 1946

LUIS MENDEZ HERNANDEZ, M.D., ACTIVE MEMBER, NATIONAL INSTITUTE OF CARDIOLOGY, MEXICO

A study was made on twenty-five patients with embolism. These included seventeen emboli to the brain, ten to the peripheral arteries, and one to the retina. The percentage among individuals with rheumatic heart disease was 1.35; among individuals with auricular fibrillation, 9.43; among individuals with with bacterial endocarditis, 5; and among those with myocardial infarction, 2.08 per cent.

The difference between peripheral embolism and thrombophlebitis cannot be easily established because both are often found in cases of rheumatic fever, auricular fibrillation, and heart failure, and both bear a very close clinical resemblance.

The differential diagnosis in cerebral involvement has been established as follows: Brain hemorrhage is seen in young patients with active rheumatic fever in whom the neurological picture is serious and not well defined. Embolism occurs in older individuals with advanced heart disease in whom hemiplegia or aphasia or both are found. In these older individuals with emboli, infection is not important.

The gravity of the vascular accident depends upon the size of the embolus, upon whether it is placed in an important artery, and upon whether there are multiple emboli in large arteries. When the latter is the case, the outcome is less favorable.

CLINICAL IMPRESSION OF THE THERAPY IN THROMBOANGIITIS OBLITERANS

TERESA MCGOVERN, M.D., NEW YORK POST-GRADUATE HOSPITAL, NEW YORK, N. Y.

This is a report on 278 patients with thromboangiitis obliterans seen during the past thirteen years in the New York Post-Graduate Hospital Vascular Clinic and in the offices of some of the group associated with the Clinic. The purpose of presenting this paper is to give our clinical impressions of the effects of therapy in these patients. The patients were carefully checked in order to rule out those who did not have true thromboangiitis obliterans. In each in-

stance, the age, sex, nationality, background, habits, and emotional status of the patient were noted.

Because the etiology of the disease is unknown, we turn to the pathology and pathologic physiology for an appreciation of what can be accomplished and expected from therapy. Thromboangiitis obliterans is a true angiitis with an associated venous thrombosis and an inflammatory lesion of the accompanying nerve. With this last factor added, we have a chain of events that makes for multiple problems; arterial, venous, arteriolar, and sympathetic, not to mention the psychosomatic. The elimination of pain, inflammation, ischemia, and gangrene are the main concern.

Our routine therapy consists of no smoking, an oscillating bed, potassium permanganate (1:5000) soaks at 90-94° F. daily for twenty minutes, typhoid vaccine intravenously, sterile dressings, protection of the limbs, heels, etc., and sedation and whiskey.

In setting up the rules for therapy, the complete elimination of tobacco has been a rigid rule. Not all patients live up to this. It has been our experience that if they do, in most patients, pain will cease and lesions will begin to heal almost from the start. On the other hand, let the patient recommence smoking and the pain will recur and lesions will become active and will not heal.

Pain, a very real problem in thromboangiitis obliterans, is markedly decreased by intravenous typhoid vaccine. In our experience, this has occurred too often to be coincidental.

The meticulous care of the feet is probably one of the most important forms of therapy. Care of the corns, nails, and calluses must be emphasized. A neglected callus or ingrown toenail may be the antecedent to an amputation.

The extremity with an open lesion needs rest. This should be physiologic in nature; that is, six inches below heart level, or "Buerger type," or that afforded by an oscillating bed; the extremity should never be elevated. We feel at present that the ideal temperature for those extremities is 80 to 84° F. Our opinions regarding refrigeration are in a state of flux. We have not been successful in saving limbs from amputation by refrigeration, once it became obvious that gangrene was inevitable. The scrupulous care of the small or early lesion is important. Protection of the extremities at all times is necessary. The patient must be taught to live within the capacity of his limited blood supply, and to carry out the therapy outlined faithfully.

We have come to the following conclusions:

1. Patients who stop smoking can be assured a remission in their disease, which can and does last for years with no need for any form of therapy other than abstinence from nicotine. No therapy, regardless of what is given or the amount, is of sufficient magnitude to overcome the bad effect of tobacco.

2. Hygiene of the feet is important. It may be that fungous infections sensitize the tissues, or that the cracks in the skin are the opening wedge for streptococcus and stephylococcus infection with their sequelae.

3. If we can educate the patients with thromboangiitis obliterans to stop smoking and live within the capacity of their impaired blood supply, no further therapy is needed.

INCIDENCE AND CLINICAL FEATURES OF RHEUMATIC FEVER IN MEXICO CITY

J. Robles Gil, M.D., National Institute of Cardiology, Mexico

The author studied the clinical characteristics of rheumatic fever in 750 patients in order to establish the special features of the disease as seen in Mexico. The incidence of the disease was computed from a careful analysis of 2,000 post-

mortem examinations, as well as from a study of the clinical records of patients observed at the Instituto Nacional de Cardiologia de Mexico.

Of the 750 patients with rheumatic disease, 66.2 per cent were women. The main symptoms were noted as follows: carditis, 93 per cent; arthritis, 61.8 per cent; chorea, 13 per cent; subcutaneous nodules, 7.8 per cent; and rheumatic erythema, 2.4 per cent. The following secondary manifestations were recorded: anemia, 57.7 per cent; joint pain, 52.7 per cent; loss of weight, 50.3 per cent; asthenia, 47 per cent; epistaxis, 26.8 per cent; adynamia, 19.2 per cent; muscular pain, 18.6 per cent; torticollis, 16.8 per cent; chest pain, 9 per cent; fever not associated with arthritis, 8.9 per cent; purpura, 2.2 per cent; and abdominal pain in 1.2 per cent. The commonest combinations of symptoms in rheumatic fever were: arthritis and carditis, 48.4 per cent; carditis alone, 32.4 per cent; carditis, arthritis, and chorea, 7.4 per cent; carditis and chorea, 5.2 per cent; arthritis and chorea, 0.2 per cent.

It could be observed that chorea appeared, on the average, in the first decade of life, while arthritis tended to appear ten years later, and carditis a little less than twenty years afterward. On the other hand, nervous (chorea) and joint symptoms remained only for months, while carditis showed activity for years.

Arthritis was recorded as the initial symptom of rheumatic fever in 50 per cent of the patients, carditis in 37.4 per cent, and chorea in 8.8 per cent. There was an average interval of eight years between the first and the second attack of rheumatic fever.

Valvular involvement occurred in the following proportions: a double mitral lesion was recorded in 52.5 per cent; mitral stenosis in 21.3 per cent; mitral disease and aortic insufficiency in 6.6 per cent; mitral and aortic involvement in 4.7 per cent; mitral insufficiency in 3.8 per cent; mitral stenosis and aortic insufficiency in 2.1 per cent; mitral and aortic insufficiency, 1.9 per cent; mitral insufficiency and aortic disease in 1.7 per cent; and aortic insufficiency alone in 1.2 per cent. The tricuspid and pulmonary valves were involved in a very small percentage of the cases.

Patients with polyarthritis gave the following symptomatology: pain in 97.8 per cent; delitescence in 96 per cent; phlogosis in 86.2 per cent; fever in 82 per cent; migration of the joint involvement in 70.9 per cent; and diaphoresis in 69.1 per cent. The involved joints were as follows: knees, 63 per cent; ankles, 58 per cent; elbows, 34.9 per cent; wrists, 31.4 per cent; fingers, 21.5 per cent; shoulder, 21.4 per cent; all joints, 20 per cent; hips, 6.3 per cent; spine, 5.7 per cent; sacroiliac, 3.3 per cent; and temporomandibular, 1.3 per cent.

Rheumatic fever appeared most often during the winter and spring months. The onset of rheumatic attacks was associated with infections due to hemolytic streptococcus in 61.7 per cent. In 87 per cent the antistreptolysin titer was found to be high, and in 38 per cent of the cases, the hemolytic streptococcus was recovered from the nasopharynx of the patients.

In 31.4 per cent of the relatives of patients with rheumatic fever there was a history of some rheumatic symptoms; in 9.8 per cent there was a definite history of rheumatic fever. No other particular disease could be found in the relatives of the rheumatic patients which could be incriminated as a predisposing factor to the rheumatic infection. Poverty, however, existed in 47.6 per cent of the patients.

Rheumatic fever is not rare in the temperate and even tropical zones of Mexico. The post-mortem incidence was 11 per cent; the figure rose to 38 per cent in the patients studied at the Instituto de Cardiologia de Mexico.

The clinical features of rheumatic fever in Mexico are much like those described in other countries. Its high incidence justifies a definite program for its control.

IS THE ORTHODOX THERAPY OF RHEUMATIC FEVER CONDUCIVE TO PSYCHOSOMATIC DISABILITY?

W. B. Adamson, M.D., Abilene, Texas

1. The nature of rheumatic fever has been briefly considered and the probability of psychosomatic or functional disability resulting inadvertently from, or at least during, the course of orthodox management of this disease has been pointed out.
2. The preventable nature of these disabling conditions is apparent.
3. Adequate therapy can probably be accomplished with a lesser period of bed rest than was formerly thought necessary.
4. Through adequate psychologic understanding and the practice of intelligent psychotherapy, we as physicians can prevent at least part of the disability resulting from rheumatic fever.

CLINICAL FEATURES OF 1,160 CASES OF RHEUMATIC VALVULAR ENDOCARDITIS

C. Cortes, M.D., and Hernan Villarreal, M.D., Active Members, National Institute of Cardiology, Mexico

The authors studied 5,665 clinical and 250 post-mortem records of patients seen up to 1946 at the Cardiological Institute. This material included 1,809 subjects without heart disease. A diagnosis of rheumatic endocarditis was made in 1,225 patients, although only 1,160 clinical records were of interest for the present study. Of all cases examined post mortem 147 displayed rheumatic endocarditis.

Analysis of these records allows the following conclusions:

1. Rheumatic endocarditis occurred in 30.9 per cent of the cardiac patients.
2. Of these, 63 per cent were women.
3. No racial characteristics which predispose to rheumatic heart disease were noted.
4. A history of rheumatic fever in consanguineous relatives was definite in 10.9 per cent of the cases and doubtful in 2.6 per cent.
5. A history of rheumatic fever was recorded in 56 per cent of the cases; a history of chorea was present in 13.1 per cent.
6. Rheumatic heart disease without a history of rheumatic fever occurred in 65.5 per cent of patients.
7. The first attack of rheumatic fever appeared between the ages of 11 and 20 years in 46.8 per cent of the cases; of those who had chorea the disease occurred between the ages of 6 and 10 years in 57.2 per cent of the cases.
8. Joint pain was the prevalent symptom of rheumatic fever (51.4 per cent); other symptoms in order of frequency were tonsillitis, 50.6 per cent; epistaxis, 28.7 per cent; torticollis, 20.3 per cent; muscular pain, 20.1 per cent; conjunctival hyperemia, 7.4 per cent; and abdominal pain, 2.8 per cent.
9. The clinical diagnosis of valvular involvement was as follows: mitral in 1,122 cases, 96 per cent; aortic in 209 cases, 18.0 per cent; tricuspid in 20 cases, 1.7 per cent; and pulmonary in none.
10. Of the 1,160 patients, 44.1 per cent had symptoms of cardiac failure.
11. Heart failure was most often seen between the second and the fourth decade of life; failure was particularly prone to develop from three to ten years, and from sixteen to twenty years after the first rheumatic attack.
12. Disturbances of rhythm were found in 203 patients, 193 with auricular fibrillation and ten with auricular flutter. Conduction disturbances were re-

corded in sixty-nine patients: forty-nine with first degree, three with second degree, three with complete A-V block, and fourteen with bundle branch block. In 97.9 per cent auricular fibrillation coexisted with mitral stenosis.

13. Rheumatic heart disease coexisted with other forms of heart disease as follows: with congenital defect, 0.5 to 0.8 per cent; with syphilitic heart disease, 8.7 to 9.9 per cent; with bacterial endocarditis, 1.5 to 2.4 per cent; and with hypertensive heart disease, 3.6 to 6.0 per cent.

14. Valvular calcification was diagnosed clinically in 0.7 per cent of the rheumatic series. The post-mortem examinations revealed calcification in 1.4 per cent.

15. Complications were diagnosed as follows: pericarditis, 1.3 to 2.0 per cent; pleuritis, 0.9 per cent; pulmonary infarct, 1.2 to 1.4 per cent; peripheral embolism, 3.5 to 4.5 per cent; and renal involvement, 2.3 per cent.

16. The average age at which death occurred was 24.5 years. The greatest mortality occurred between 11 and 40 years of age, and particularly between 11 and 20 years of age (38 per cent).

17. The most frequent cause of death was cardiac failure (72.7 per cent).

18. Lack of correlation between clinical diagnosis and post-mortem findings was essentially due to the large incidence of tricuspid lesions (33.3 per cent); only 8.1 per cent of these were diagnosed clinically.

19. The complications found at post-mortem examination were pericarditis, 29.9 per cent; renal infarct, 27.8 per cent; pleuritis, 19.7 per cent; splenic infarct, 17 per cent; intracardiac thrombosis, 12.2 per cent; cerebral hemorrhage, 10.8 per cent; bacterial endocarditis, 8.8 per cent; and cerebral embolism, 8.1 per cent. Most of these complications coexisted with mitral valvular involvement, particularly mitral stenosis.

20. Mistakes in diagnosis as proved by the post-mortem examinations were twelve (8.1 per cent). Most often a mitral lesion was confused with aortitis or cardioangiosclerosis.

21. Among 127 patients over 44 years of age, the most common lesions found were mitral stenosis and mitral disease.

22. Since syphilis coexisted frequently in this older group of patients (23.6 per cent proved and 28.3 per cent doubtful) and since most erroneous diagnoses occurred in this same group, it is emphasized that in older patients the history as well as all clinical manifestations must be carefully considered before a final diagnosis of the nature of the valvular disease is made.

ENCEPHALOPATHY OF THE RHEUMATIC PATIENT

Alfonso de Gortari, M.D., Ruben Pellon, M.D., and Isaac Costero, M.D., Active Members, National Institute of Cardiology, Mexico

The authors describe thirty-two patients in the children's ward at the National Institute of Cardiology who had encephalitic symptoms during the course of rheumatic fever. Two types of symptoms were noted: in the first type sudden coma developed and was followed by death; in the second, psychomotor instability, obnubilation, and disturbances of sleep were observed. This state may continue for several days, often ending in sudden death.

Of one hundred fifty-one cases of rheumatic fever which were studied post mortem, 107 of the patients had pathologic changes involving the brain. Thirty-two of these were children. The encephalitic changes consisted of edema, swelling and wet appearance of the brain tissue, hyperemia, punctiform hemorrhages, and free liquid. In a large percentage there was no parallelism between peripheral and brain changes.

The changes found are not considered as specific for rheumatic fever, for they occur in many other infectious and toxic states and in conditions associated with anoxia. Cranial hypertension is thought to be the immediate cause of death. The authors propose the name rheumatic encephalopathy to describe the symptomatology. By way of treatment massive doses of oxygen are recommended, as well as all other known general measures.

THE SIGNIFICANCE OF INTERSTITIAL LYMPHOCYTOSIS IN RHEUMATIC DISEASE AND IN OTHER INFLAMMATORY PROCESSES

Isaac Costero, M.D., National Institute of Cardiology, Mexico

Rheumatic disease behaves in a very different manner in young people and in adults. It can, therefore, be considered that the disease has, in common with other diseases with an intense allergic component such as tuberculosis, two well-defined periods. The first or initial period, which tends to be prevalent in children and adolescents, has as its characteristic features severe changes in the small vessels, a subacute course, and production of death as a consequence of encephalitic changes (rheumatic encephalopathy, described by Gortari, Pellón, and Costero). The second period is seen when the disease is well established and occurs in adults. This stage is distinguished by the presence of lesions affecting mainly the endocardium, the large vessels, and the serous membranes of the joints. It runs a chronic progressive course and tends to recur. The second stage often follows the initial period and frequently leads to heart failure.

Corresponding to these two symptomatic types, rheumatic disease presents two different types of anatomic lesions: (1) Aschoff nodules and equivalent inflammatory granulomas which are abundant during the initial period and which represent a hyperergic reaction, and (2) lymphocytic infiltrations within the affected organs which are seen during the second period of the disease and are of unknown significance. It is the aim of the present work to suggest an anatomic and physiologic basis for the existence of such lymphocytic infiltrations.

1. Lymphocytic infiltrations are generally considered to represent a chronic inflammation. It is important, however, in order to facilitate the interpretation of this phenomenon, to distinguish genuine inflammation from spurious inflammation. Genuine inflammations are those which are accompanied by clinical symptoms suggesting infection, by lymphangitis, lymphadenitis, septicemia, toxemia, sapremia, and by other manifestations such as fever, antibody formation, changes affecting the white blood cells, and an increase in the blood sedimentation rate.

In spurious inflammations there are usually no manifestations of infection nor general alterations such as fever, antibody formation, and white blood cell changes. If these alterations are present in spurions inflammations, they are of subclinical intensity and are discovered only after careful investigation. The spurious type of inflammation may be divided into two different groups: (1) The so-called physiologic inflammation (Rössle) which is present during digestion and menstruation, and (2) the changes that accompany repair of inflammation following parenchymatous atrophy and those that develop where compensatory hyperplastic reactions occur, as, for example, in hydronephrosis following sudden obstruction of the ureter.

Genuine inflammation is not accompanied by lymphocytic infiltrates prior to the initiation of regenerative phenomena. In so-called physiologic inflammation the lymphocytic infiltrate constitutes the main feature of the anatomic lesion, and in the healing stage of inflammation it is frequently the only change found.

2. The phenomena of inflammation can be divided into three different types: alterative, exudative-infiltrative, and proliferative (Lubarsch). These phenomena are probably produced by the action of diffusible substances formed by disintegration of tissue and receive the names of phlogotoxins, phlogoangins, and phlogotrophins (Costero). Phlogotoxin corresponds to Menkin's necrosin; similarly, phlogoangins correspond to Menkin's leucotaxine and leucocytosis-promoting factor, as well as to the H substance of Lewis and Grant; phlogotrophins have not yet been isolated.

3. The endothelium of blood and lymphatic capillaries is impermeable to proteins of large molecular weight. Lymph contains a large amount of protein of large molecular weight. Our present knowledge suggests that proteins in the lymph are derived from cellular substance.

4. (1) Cellular extracts as well as some complex proteins behave experimentally as lymphocytogenic substances and provoke reticular hyperplasia (Wiseman). (2) Reticular cells control the metabolism of proteins of large molecular weight. (3) Under normal conditions, lymphocytes arise from reticular cells of the lymphadenoid tissue. One may suggest, in the light of these facts, that nodal lymphopoiesis is a response to proteins carried from the tissues to the nodes by the lymph.

5. In inflammation, the lymphocytic infiltrate is derived from local histiocytes (Mollendorff, Siegmund, Klinge, Maximow, Downey and Weidenreich, etc.), which may be considered homologous to the reticulum cells of the lymph nodes. Local lymphopoiesis must be stimulated by proteins derived from cells undergoing regressive or regenerative changes which alter protoplasm. This statement is borne out by (1) the relationship between the intensity of cellular repair and the degree of lymphopoiesis; (2) the increase of local lymphopoiesis when normal flow of lymph is made difficult, as in lymphadenitis; (3) the interdependence between local lymphopoiesis and the presence of pathogenic organisms; (4) the impossibility of avoiding the development of elephantiasis in lymphatic edema. When purely lymphocytic infiltrations are found within the tissues, one cannot speak of genuine inflammation, since local or generalized manifestations of inflammation are absent. This occurs during hydronephrosis following obstruction of the ureter, in diffuse glomerulonephritis, in atrophic cirrhosis of the liver, etc., when the anatomic lesions of the tissue are duly compensated. The static period of rheumatic disease belongs to this variety of spurious inflammation.

6. In rheumatic disease, as in other inflammatory processes, the lymphocytic infiltrates represent an index measuring the intensity of local cellular destruction. This is not related to the degree or the presence of pathogenic organisms or to any other cause of inflammation.

7. Since in the second stage of rheumatic disease local lymphocytic infiltrations are constantly present, one has to suspect the existence of permanent metabolic changes within the affected tissues. These metabolic changes are manifested not only by local lymphopoiesis, but also by proliferative phenomena with histiocytic proliferation. The differentiation of histiocytes results in a blockade by changes in the histiocytic system. This blockade leads to a remarkable diminution of the defensive capacity of the histiocytic system and local infections are thus facilitated. This is the rule in patients with rheumatic disease. On the other hand, complications of the same type have been observed in elephantiasis and in many other pathologic processes accompanied by local lymphocytosis and differentiation of histiocytes.

8. Infectious diseases never leave persistent metabolic alterations in the tissues. Such alterations are seen only in allergic diseases and in some infections

produced by filtrable viruses. In such cases and in rheumatic disease, the anatomic lesions may be interpreted as a form of premature autochthonous aging of the system or systems affected by the disease.

ON THE INTRAVENOUS USE OF MORPHINE IN THE TREATMENT OF PAROXYSMAL VENTRICULAR TACHYCARDIA

L. GONZALEZ SABATHIE, M.D., OFFICIAL DELEGATE, ARGENTINA

A case of ventricular paroxysmal tachycardia, which was not affected by intravenous quinidine, promptly responded to morphine administered intravenously. Since this observation, the author has used the drug routinely in all cases of ventricular paroxysmal tachycardia. The author points out that patients with paroxysmal ventricular tachycardia suffer some degree of peripheral collapse which makes the absoprtion of morphine, given subcutaneously, uncertain. Of ten cases reported, nine of the patients responded to morphine treatment. The dose varied between 1 and 4 centigrams of morphine; the interval between doses was one-half to two hours. Favorable effects were observed from ten to thirty minutes after the injection. No undesirable effects were produced. A very hypnotic action of drug was observed.

The only instance in which morphine failed to give relief was in a patient in coma with severe peripheral collapse, who had been treated unsuccessfully with quinidine. The patient died thirty-six hours after coming under the author's observation.

DIGITALIS AND QUINIDINE IN THE TREATMENT OF AURICULAR FIBRILLATION

S. A. WEISMAN, M.D., LOS ANGELES, CALIF.

The value of quinidine in the treatment of acute and chronic auricular fibrillation is fairly well established. Perhaps not enough emphasis has been put upon the part digitalis plays (1) in the preparation of the heart before starting with quinidine; (2) during the active use of quinidine in attempting to establish normal rhythm; and (3) after the irregular heart has been restored to normal rhythm.

It is the purpose of this paper to emphasize the importance and value of using both of these drugs for the most beneficial results in the treatment of auricular fibrillation.

FAGARINE—A NEW DRUG FOR THE TREATMENT OF AURICULAR FIBRILLATION AND FLUTTER

ALBERTO C. TAQUINI, M.D., VICE PRESIDENT, CARDIOLOGIC SOCIETY OF ARGENTINA, ARGENTINA

Experimental studies made with fagarine have demonstrated that this drug increases the fibrillation and flutter threshold and can make auricular fibrillation disappear in the exposed heart.

Satisfactory results have been obtained in men with auricular fibrillation and auricular flutter of rheumatic, coronary, or hypertensive origin, with doses of fagarine between 0.08 and 0.10 Gm. administered in one dose by the intramuscular route. Some patients under the influence of digitalis have shown, however, some toxic symptoms.

The present study reports pharmacologic findings in experiments made in twenty-five normal individuals to whom the drug was administered in doses of

0.50, 0.60, 0.75, and 0.85 Gm. (1 centigram per kilogram of body weight) alone, or after atropine or complete digitalization.

Drug effects were studied clinically and electrocardiographically. No toxic symptoms were noticed. Electrocardiograms showed in all cases a definite increase of S-T interval with depression of this segment and of the T wave. These changes were proportional to the amount of drug employed. When atropine was given intravenously in doses of 1 mg., the electrocardiographic effects of fagarine were reduced in most of the cases. When fagarine was administered after the use of digitalis, in doses of 1 centigram per 5 kg. of body weight, the electrographic changes were accentuated.

Since fagarine in doses as small as 0.005 Gm. per kilogram of body weight has a definite effect on the heart muscle, it is concluded that a therapeutic assay should be started with this dose which is far below the toxic level. Special precautions should be taken in the case of patients who are under the influence of digitalis.

POST-TACHYCARDIA SYNDROME

Pedro Cossio, M.D., and Isaac Berconsky, M.D., Active Members
Medical Faculty of Buenos Aires, Argentina

Certain cases of paroxysmal tachycardia deserve consideration because of clinical and electrocardiographic characteristics even though these cannot be explained upon an anatomic basis.

These characteristics, which make up the post-tachycardia syndrome, are as follows: (1) It is often seen in relatively young individuals without organic heart disease. (2) It is seen with prolonged and repeated bouts of paroxysmal tachycardia, commonly of ventricular origin. (3) Reversible cardiac enlargement occurs. (4) Depression of S-T, inversion and widening of the T wave, and prolongation of the Q-T interval, especially in Leads I, II, CR_4, CR_5, and CR_6, are recorded immediately after the attack or some hours later. (5) Electrocardiographic changes regress progressively over a period of several days. (6) Hypertrophy and dilatation of the heart with absence of any other important myocardial lesions are found at post-mortem examination.

Even though the post-tachycardia syndrome is not accompanied by histologic changes affecting the heart, it must not be considered harmless; death can occur suddenly from heart failure.

AURICULAR PREFIBRILLATION

L. Gonzalez Sabathie, M.D., and Fernando Gaspary, M.D.,
Official Delegates, Argentina

The authors report a study of sixty patients during the past nine years in whom there was a disturbance in auricular activity that preceded the onset of auricular fibrillation. A classification is proposed to describe auricular prefibrillatory disturbances. Prefibrillation P waves may be the only manifestation or they may be associated with: (1) auricular extrasystoles (of the common type, totally or partially blocked, isolated, or with short runs of tachycardia); (2) auricular tachycardia (paroxysmal, or of the common type, or atypical); (3) auricular "anarchy" and polymorphism of P waves; (4) auricular flutter.

Prefibrillation P waves show an alteration in height, width, or contour. Such changes may occur as an isolated or as a recurring phenomenon. Different morphologic types are described and are more important if found in the peripheral leads in patients with organic heart disease who have cardiac enlargement.

An auricular extrasystole acquires the characteristic of a prefibrillation disturbance if it occurs where prefibrillation P waves are present. Auricular extrasystoles frequently present varying degrees of block, the commonest being increase in the P-R interval. In some instances there are runs of auricular extrasystoles. Tracings are presented to show the importance of auricular extrasystole in determining the onset of auricular fibrillation.

Auricular tachycardia may be considered to be of (1) the common type and (2) the atypical type. These types may be recognized by the exceptional or the normal pattern of the P waves.

Polymorphism of the P wave is an intermediary degree between auricular extrasystole and auricular anarchy and is characterized by the presence (in the same tracing) of auricular waves with variable size and direction, and with irregular ventricular rhythm.

Auricular anarchy is defined as the greatest degree of polymorphism of the P waves. It is difficult to find the basic pattern. Clinical identification is impossible but complete arrhythmia exists and the electrocardiogram reveals that each ventricular complex is preceded (in a variable amount of time) by P waves of variable width, height, and form.

Auricular flutter is considered a prefibrillation form. The study of auricular prefibrillation shows disturbances of intraauricular conditions, auricular excitability, and hypertrophy of auricular muscle with distention or dilatation.

Experimental and clinical studies of the factors which lead to auricular fibrillation was purposely made in order to interpret the mechanism and significance of prefibrillation auricular disturbances. Several factors such as anoxemia, vagal action, auricular distention and dilatation, and structural lesions of the auricle were considered.

The conclusion is reached that the study of prefibrillation auricular disturbances gives support to the idea that auricular fibrillation is a result of irregular and multiple returning stimulations, having their origin in multiple premature auricular excitations with multiple regional and changing blocks.

Evolution and prognosis of prefibrillation auricular disturbances depend on (1) the type of disturbance, (2) the etiological factor involved, and (3) the efficiency of the treatment.

THE PATHOGENESIS AND TREATMENT OF HYPERTENSION

Arthur Grollman, M.D., Southwestern Medical College,
Dallas, Texas

Recent studies on experimental hypertension are reviewed in an attempt to evaluate the most likely hypothesis explaining the probable pathogenesis of chronic hypertension. The inadequacy of the pressor theory or renin hypothesis to explain the known facts is shown. An alternative hypothesis, in which the normal kidney is assumed to elaborate an essential metabolite in the organism, is in accord with the known experimental data. The application of these studies to the practical management of hypertensive cardiovascular disease is presented.

CRITICAL EXAMINATION OF THE CURRENT CLASSIFICATION OF THE LOCALIZATION OF MYOCARDIAL INFARCTS (THE AUTHOR'S TERMINOLOGY)

GUILLERMO BOSCO, M.D., ACTIVE MEMBER, FACULTY OF MEDICAL SCIENCES OF BUENOS AIRES, ARGENTINA

Although it is generally accepted that infarction of the heart develops most often in the left ventricle, the author claims that the anatomicoclinical nomenclature proposed by him in 1936 makes it possible to localize the infarct more exactly. Furthermore, it makes possible a more accurate clinical and differential diagnosis, as well as prognosis. What has been described as infarction of the right ventricle is no more than an extension from the left ventricle caused by occlusion of that variety of left circumflex artery which has a distribution to the posterior wall of the right ventricle. This infarct is called the "anomalous type" (20 per cent of the cases).

A notorious confusion in the anatomicotopographic facts has resulted in many different names for infarcts according to their localization: for example, anteroapical; posterobasal; midventricular; undetermined; combined; atypical; anteroposterior; anterior, extensive; anteroseptal; anterolateral; laterobasal; posterolateral; posteroinferior; and multiple. On the contrary, the author states that according to his terminology the infarct is located in 80 per cent of the cases in the lateral, anterior, or posterior walls of the left ventricle, extending in some 20 per cent to the posterior wall of the right ventricle, but always being produced by the obliteration of branches of the left coronary system and never by obliteration of the right coronary artery.

The author attributes erroneous classifications to a disregard of the myrocardial, pericardial, endocardial, and special conducting regions dependent on given arteries ("topographic myocardiovascular territories"). Upon such a basis and upon verification of anatomic, anatomicophysiologic, clinical, and electrocardiographic facts, the author was able to build up an anatomicoclinical nomenclature of infarction in the heart. This includes three syndromes which he names lateral, anterior, and posterior, depending, respectively, on oblitaration of the left circumflex of short extension (not reaching the right ventricle), of the anterior descending or "normal type," and of the left circumflex of great extension or "anomalous type" (reaching the right ventricle). In referring to each syndrome, the author describes the pathologic changes, the symptoms, and the specific electrocardiographic patterns. Emphasis is also given to the mechanism of production and to the diagnostic, topographic, clinical, differential, and prognostic value of the systolic murmur, the pericardial friction rub, paroxysmal tachycardia with left ventricular extrasystoles, complete or incomplete auriculoventricular dissociation, right bundle branch block, partial left bundle branch block, and monophasic deviation of the S-T segment.

TREATMENT OF ACUTE CORONARY THROMBOSIS WITH DICUMAROL: FURTHER OBSERVATIONS

E. STERLING NICHOL, M.D., MIAMI, FLA.

The author has treated all private patients with acute coronary thrombosis seen by him between June, 1943, and June, 1946, with dicumarol in the hope of preventing thrombosing and embolic complications and thus reducing the death rate as well as lessening the morbidity. At the start of this therapeutic experiment it was hoped that the proper use of dicumarol would forstall the formation of mural (intracardiac) thrombi and subsequent embolic showers; the experience

thus far has confirmed this expectation. Added benefits of dicumarol treatment consist in the presumptive prevention both of extension of the initial coronary thrombus by propagation, as well as the formation of new thrombi in other coronary branches. (Multiple thrombosis is an intriguing phenomenon and its importance has been recognized in recent years without a satisfactory answer as to its causation.) Another important way in which dicumarol may benefit these patients is by preventing pulmonary embolism deriving from thrombosed veins in the legs and pelvis, since the majority of massive, fatal pulmonary emboli occurring in the course of acute coronary thrombosis have their origin in the deep veins rather than in the right ventricle.

A total of sixty-eight attacks occurring in sixty-two patients have been treated with dicumarol thus far, but the present report includes the data on forty-four patients reported last January by the author and his former associate, Dr. Samuel W. Page, Jr. Fifty of the group treated were 49 years of age or older with ages ranging from 38 to 81 years. There were forty-one men. The acute episodes were classed as severe forty-three times. There were thirty-eight first attacks, twenty-five second attacks, and five third attacks.

Results: There were eleven deaths, giving a mortality rate of 16 per cent, but since three patients expired before the prothrombin time could be altered significantly, it is justifiable to depict the mortality rate as 12 per cent of sixty-five attacks. In the thirty-eight first attacks, there was only one death, giving a mortality rate of less than three per cent in initial attacks.

Of the sixty-eight episodes studied, in only one was there any clinical evidence of pulmonary embolism after dicumarol therapy was started and this was not clear-cut, since the patient died in congestive failure and no autopsy was granted. Mesenteric artery embolism was found at autopsy in one patient, but the source was an atheromatous aortic plaque, since there was no mural thrombus present. No other systemic emboli were encountered clinically.

In none of the eight autopsied cases was there any evidence of mural thrombi, or pulmonary or systemic embolism (except for the instance in which the origin was in the atheromatous lesion). One patient, not autopsied, died from a cerebral accident which may have been hemorrhage, but he was found to be uremic shortly after dicumarol therapy was started and should not have received the drug, since renal impairment of severe degree is a contraindication. Another patient, a physician 81 years of age, who died fourteen days after beginning therapy, showed a ruptured left ventricle at autopsy with the usual intrapericardial hemorrhage. There was no evidence of undue hemorrhage or liver damage ascrible to dicumarol in the eight autopsied cases.

Peters and associates last April reported only two deaths in fifty patients similarly treated. This contrasted to thirteen deaths in a control group of sixty patients. Wright recently reported encouraging experiences in seventy-six similar patients given dicumarol. In both of these series, as well as in the present study, other common modalities of treatment were employed.

IMPORTANCE OF PRECORDIAL LEADS IN ELECTROCARDIOGRAMS AFTER EXERTION IN ANGINA PECTORIS; ACTION OF CERTAIN DRUGS (TRINITRIN, AMINOPHYLLINE, AND PAPAVERINE)

ANTONIO BATTRO, M.D., AND EMILIO ARAYA, M.D., NATIONAL ACADEMY OF MEDICINE, ARGENTINA

The effects of exercise on the electrocardiogram were studied in sixty-four individuals. These included twenty-six normal persons, thirty patients with angina pectoris, and eight patients who had had cardiac infarction which was not followed by anginal episodes.

The following studies were made in every patient: (1) Leads I, II, and III, and precordial leads CF_1, CF_2, CF_3, CF_4, CF_5, and CF_6 were recorded before and after exercise. (2) The behavior of blood pressure, the pulse rate, and the presence of subjective symptoms were observed during exertion. (3) The effect of certain drugs (trinitrine, aminophylline, and papaverine) upon the electrocardiogram before and after exertion and upon arterial blood pressure were observed.

None of the normal subjects showed a significant electrocardiographic response to exercise. In contrast, 80 per cent of the patients with angina pectoris showed a positive response. In 20 per cent of these positive reactors the change occurred in the precordial leads.

When deviation of S-T segment followed exercise, it was usually observed in Leads CF_1, CF_2, and CF_3. When exercise produced inversion of the T wave as well as deviation of the S-T segment, this change was usually noted in Leads CF_3, CF_4, CF_5, and CF_6.

CARDIAC PAIN

Don C. Sutton, M.D., Northwestern University, Chicago, Ill.

Cardiac pain is caused by a relative or absolute ischemia of a part or all of the myocardium.

The ischemia is caused by (1) great stress or overwork of the normal heart; (2) rapidly beating heart, as in hyperthyroidism, paroxysmal tachycardia, or auricular flutter; (3) impoverishment of the blood, as in anoxemia, anemia, or hypoglycemia; (4) disease of the coronary arteries; (5) mypoplasia and anomalies of the coronary artery; and (6) spasm due to vagal reflexes.

Theories of cardiac pain, such as the stretching of the aorta, as held by Vacquez, and myocardial fatigue, as discussed by Mackenzie, are considered. Experimental evidence of diminished blood flow to the myocardium as the result of organic narrowing of a coronary artery or reflex spasm are critically examined. Cardiac pain is considered to be entirely the result of ischemia from the causes mentioned.

It is important for the clinician to differentiate the causes of cardiac pain: (1) Cardiac pain resulting from coronary artery sclerosis depends on other evidence of arteriosclerosis, especially electrocardiographic changes. (2) Pain as the result of artery spasm is usually reflex from the lung or abdominal viscera. Vagel reflex spasm is relieved or diminished by full doses of atropine. (3) The radicular syndrome from lesions of the lower cervical or upper dorsal vertebrae may simulate anginal pain very closely.

HERNIA OF ESOPHAGEAL-HIATUS: ITS RELATIONSHIP TO ANGINA PECTORIS

Franklin R. Nuzum, M.D., Santa Barbara, Calif.

1. One hundred private patients in whom a diagnosis of angina pectoris had been made were studied by x-ray to determine the presence of hernia of the esophageal hiatus. Twenty-five such hernias were found, twenty-two of the small type and three of the large type.

2. Six of this group of twenty-five patients with hiatus hernia had the symptoms relieved by medical management. A seventh, with a typical picture of angina pectoris, was relieved of all symptoms following surgical repair of a large hiatus hernia.

3. One patient, followed for a period of fourteen years, had probably a hiatus hernia at first and added coronary disease later. This instance is cited to emphasize the point that both conditions may occur together.

4. Another patient, complaining of pain beneath the lower third of the sternum radiating to the left shoulder, had a large hiatus hernia 9 cm. in diameter and a hemoglobin of 46 per cent. Bleeding points or ulceration within the hiatus hernia have been recorded in 11 per cent of one group of patients reported in the literature. In such instances correction of the anemia often relieves the symptoms.

5. A control group of 957 patients who received x-ray study of the gastrointestinal tract, in which a search for hernia of the esophageal hiatus was a routine part of the procedure, were found to have hiatus hernia to the number of seventy-eight, or 12.27 per cent. The highest incidence reported in any other control group is 3 per cent.

RESULTS OF SURGERY IN PATENT DUCTUS ARTERIOSUS

M. J. Shapiro, M.D., University of Minnesota, and Evelyn Johnson, M.D., Minneapolis Children's Heart Hospital and Clinic, Minneapolis, Minn.

1. An analysis of 643 patients who underwent operations for patent ductus arteriosus by forty-six surgeons has been presented.

2. Six hundred twenty-six individuals were found to have a patent ductus at operation, 525 were uninfected and 101 were infected. In seventeen instances the diagnosis was incorrect.

3. The mortality rate in ligation of the uninfected duct was 4.9 per cent. However, 8.7 per cent resulted in recanalization.

4. Ligation of the duct is now obsolete and should be done only where section is impossible. That section of the duct is a safe and practical procedure is established by the fact that 172 patients with uninfected patent ductus arteriosus have been so treated without a single fatality and no recanalization.

5. Errors in diagnosis will be less frequent if only patients with the typical machinery murmur are subjected to surgery.

THE DIFFERENTIAL DIAGNOSIS OF AORTIC STENOSIS, PULMONARY STENOSIS, PATENT DUCTUS ARTERIOSUS, AND COARCTATION OF THE AORTA

W. J. Kerr, M.D., University of California, San Francisco, Calif.

The purpose of this paper is to discuss the differential diagnosis of the following clinical conditions involving the cardiovascular system: (1) aortic stenosis, (2) pulmonary stenosis, (3) patent ductus arteriosus, and (4) coarctation of the aorta.

Clinical diagnosis of these states is now possible if one takes into account the location and the timing (time relationships) of the thrills and murmurs with respect to the first sound at the apex. This can be done by using the symballophone which makes it possible to compare the time of appearance of two sounds of similar or dissimilar qualities.

Thrills and murmurs originating in the circulatory system travel in both directions, but travel a greater distance in the direction of the blood flow. They travel peripherally on the pulse wave; the rate at which they progress is determined by the level of the diastolic pressure. Roughly, the waves travel at the rate of 10 to 15 meters per second, which increases as the pulse wave approaches

the periphery in the arterial system. If the thrills and murmurs travelled as sound waves, they would travel from 100 to 200 times as fast as they actually travel.

Aortic Stenosis.—The systolic thrill and murmur are located adjacent to the right border of the sternum and at that point are synchronous with the first sound. They are propagated along the course of the aorta and great vessels of the systemic circuit. They appear later than the apex impulse and the first sound at the apex, and the greater the distance from the heart, the greater the delay in time of appearance. They can be shown to be synchronous with the pulse wave.

Pulmonary Stenosis.—The systolic murmur is found adjacent to the sternum on the left in the second intercostal space. It is synchronous with the first sound and is not transmitted beyond the thorax. Its pathway follows the pulmonary artery. Its intensity is more marked in the upper part of the chest on the left because the left pulmonary artery is more superficial than the right branch, which lies behind the ascending limb of the thoracic aorta. If one compares the timing of the systolic murmur at some point distant from the pulmonary valve with the first sound, its appearance will be somewhat later than the first sound.

Patent Ductus Arteriosus.—This congenital anomaly generally shows the characteristic continuous murmur with the so-called "systolic accentuation." The thrill and the accentuated phase of the murmur are found in the same location as in pulmonary stenosis, but they appear much later than the first sound at the apex, because the pulse wave must pass through the ascending limb and arch of the thoracic aorta and through the ductus arteriosus before the accentuated phase is produced. This delay in timing is sufficient to establish the diagnosis.

Coarctation of the Aorta.—The so-called "systolic murmur" is heard in the upper dorsal thoracic region adjacent to the spine. The murmur actually is not produced until the pulse wave in the thoracic aorta has reached the narrowed channel at the site of coarctation. Therefore, the difference in timing with the first sound at the apex is notable and can be determined easily by the methods discussed.

REPORT OF A CASE OF TRICUSPID INSUFFICIENCY OF THE EBSTEIN TYPE WITH PROBABLE FETAL ENDOCARDITIS AND EXCEPTIONAL ELECTROCARDIOGRAPHIC CHARACTERISTICS

SAMUEL BERBER, M.D., OFFICIAL DELEGATE, CHILDREN'S HOSPITAL OF MEXICO

The nineteenth case of tricuspid insufficiency of Ebstein's type is reported. It has as special features fetal endocarditis caused by rheumatic fever of the mother during pregnancy and an electrocardiogram with retrograde P waves following the initial ventricular deflections. It is concluded that the defects observed were developmental in origin and that the valvulitis was superimposed. The electrocardiographic features are explained on the basis of a retrograde activation of the auricles through the intimal union between leaflets of the tricuspid valve and the ventricular wall.

CLASSIFICATION OF CONGENITAL HEART DISEASES

Perez de los Reyes, M.D., Vice President, Cuban Society of Cardiology, and Augustin Castellanos, M.D., Official Delegate, School of Medicine of Havana, Cuba

The authors have made a critical study of the different classifications of congenital heart disease from those of Pezzi and Laubry up to that of Cossio. The clinical, angiocardiographic, and anatomicopathologic analysis of the author's material from 1935 forms the basis for a new classification that takes account of previous work on the subject and tries to avoid former errors and omissions, which are to be explained by lack of the resources of modern methods of clinical investigation that the cardiologist now possesses. It is the purpose of this new classification to facilitate the task of clinicians, pediatricians, cardiologists and radiologists in diagnosis.

There is used for the first time in medical literature the word "biologia," meaning the association of two congenital defects, such as pulmonary stenosis or atresia with interventricular communication, or association of the latter with interauricular communication. In the first example, pulmonary stenosis with interventricular communication, the authors establish three degrees of biologia: type I, type II, and type III.

The authors introduce in the subgroups microcardia, formerly neglected, and the abnormalities of the vena cava. They also point out that agenesia of some of the branches of the pulmonary artery, such as are found in lack of development of the lung, are to be considered in the classification.

It is stated that this classification has as its basis not only clinical and electrocardiographic findings, but also the findings revealed by angiocardiography and the data obtained in post-mortem examinations.

Angiocardiographic technique has permitted the correction of many diagnoses that would have been made incorrectly if there were taken into consideration only the findings revealed by the usual clinical methods.

CARDIAC FAILURE IN TRICUSPID DISEASE

Alberto C. Taquini, M.D., Official Delegate, Argentine Society of Cardiology, Argentina

The author studied nine patients with rheumatic disease with involvement of the tricuspid and the mitral valves, with the aim of investigating the fundamental cause of the dyspnea. The following tests were performed in each case: lung ventilation, lung volume and its divisions, alveolar air, oxygen consumption, oxygen difference between arterial and venous blood, blood velocity, and blood volume.

The following results were obtained: Minute output was found normal in all patients without heart failure and was lessened in patients with heart failure. As is seen in other forms of heart disease, the dimininution of the minute output corresponded to the degree of cardiac failure. Blood volume was increased in all patients, even in the absence of cardiac failure. Lung ventilation was augmented in most patients in proportion to the degree of cardiac failure. Oxygen consumption proved to be above the normal level. Oxygen and carbon dioxide equivalents were found diminished in relation to hyperventilation and increase in oxygen intake. Vital as well as total lung capacity was decreased; residual air remained within normal limits. No correspondence was found between venous pressure or blood velocity or arteriovenous oxygen difference

and lung ventilation. On the contrary, it was observed that the respiratory changes in tricuspid disease are comparable to those known to occur in mitral involvement.

It is therefore concluded that dyspnea in tricuspid disease of rheumatic origin has to be attributed mainly to the coexistence of mitral pathology.

A NEW DIAGNOSTIC SIGN OF TRICUSPID INSUFFICIENCY

J. M. RIVERO CARVALLO, M.D., ACTIVE MEMBER, NATIONAL INSTITUTE OF CARDIOLOGY, MEXICO

Post-mortem studies made at the Instituto Nacional de Cardiologia de Mexico have shown that the incidence of real tricuspid insufficiency with functional disturbance is 33.3 per cent, and that the incidence of functional insufficiency is 5.44 per cent, a total incidence of 39 per cent.

Since valvular lesions of the tricuspid valve are difficult to diagnose, a new sign that may facilitate the clinical diagnosis of tricuspid insufficiency is described.

The new sign consists in producing a tricuspid murmur in patients in whom no murmur is heard, or in increasing the intensity of a previously heard murmur by having the patient take a deep inspiration or hold his breath after a deep inspiration. A very short period of apnea such as occurs when children cry may be enough to make the acoustic change noticeable. In some patients the characteristic murmur can be noticed during normal inspiration. The increased intensity of the murmur may or may not be associated with changes in pitch. The intensity is almost always increased; in some patients, however, the murmur does not change in intensity. Even when the intensity is not increased, the sign is of value since the intensity of other cardiac murmurs may be diminished by the procedure. The site of maximum intensity of the tricuspid murmur is usually the tricuspid area, but the site may be changed either to the right or left of the sternal bone; there were cases recorded in which the murmur was heard loudest close to the apex.

The new sign seems to be present in 90 per cent of patients with tricuspid insufficiency. The new sign is considered to be rarely absent in proved cases of tricuspid insufficiency.

EXPERIMENTAL STENOSIS OF THE PULMONARY ARTERY

R. F. VACCAREZA, M.D., LANARI CROXATTO, M.D., AND V. J. ALBERTI, M.D., ARGENTINA

Stenosis of the pulmonary artery was surgically produced which reduced the lumen of the vessel at least 50 per cent. Hypertension of the corresponding territory followed the operation and aortic and pulmonary blood pressures were recorded with a Hamilton manometer during the operation, and changes in pressure that developed after operation in the pulmonary and general circulation were followed. The effects of the hypertension on the weight of both ventricles and the diameter of the myocardial fibers were studied. To accomplish the latter study, a small piece of muscle was removed at the first operation.

ANGIOGRAPHY OF THE AORTA

C. GOMEZ DEL CAMPO, M.D., AND J. MENESES HOYOS, M.D., OFFICIAL DELEGATES, CENTRAL MILITARY HOSPITAL OF MEXICO, MEXICO

A new method of arteriography of the thoracic aorta has been successfully used by the authors. Good roentgenograms of the thoracic aorta, its main branches, the arteries of the neck, and the coronary vessels were obtained by means of direct injection of opaque solutions into the aortic arch.

BENIGN RESIDUAL ARRHYTHMIAS

LUIS GONZALEZ SABATHIE, M.D., AND FERNANDO GASPARY, M.D., OFFICIAL DELEGATES, MEDICAL SOCIETY OF ROSARIO, ARGENTINA

Two fundamental observations have led the authors to describe the so-called benign residual arrhythmias. The first was the appearance of coupled ventricular extrasystoles during the course of a severe attack of influenza in a woman 30 years of age, who was known before this illness to be normal from the cardiologic standpoint. Although the infectious disease disappeared, the disturbance in rhythm has persisted without change for fifteen years, without any other manifestation of heart disease.

The second observation was the appearance of second degree A-V heart block in four young persons who had been under observation for a long period of time (two to fifteen years); in these individuals the arrhythmia has been the only expression of cardiac abnormality. Search for etiological factors was carefully made without any result, and the evolution of the disturbance has shown it to be harmless.

From these observations the conclusion has been reached that there exists a group of arrhythmias which are of benign character. The different types of arrhythmias belonging to this category are the following: ventricular and auricular extrasystoles; bigeminal ventricular extrasystoles; simple increase in the conduction time; temporary A-V block and other forms of incomplete A-V block; intraventricular blocks; and paroxysmal auricular fibrillation (present in one patient for twenty years).

Reference is made to the frequency with which some infectious or parasitic diseases produce myocardial lesions. It is suspected that many disturbances of the cardiac system of unknown cause, including the benign arrhythmias that have been referred to, have their origin in inactive fibrous scars left by old myocarditis. In myocarditis total recovery may occur, or in the case of necrobiosis, scar tissue can be formed with areas of interstitial fibrosis that may constitute a definite obstacle for the conduction of the stimulus, or a permanent factor of irritation. The fibrous lesions, a result of acute inflammatory changes affecting the heart muscle, have been very well known to pathologists for a long time, but their presence has been ignored by clinicians.

Knowledge of residual benign arrhythmias has a very useful value from the practical standpoint, because their prognosis is excellent, there is no tendency to progression, and there is little or no response to therapeutic measures. The patients with benign residual arrhythmias have very few or no symptoms, and in many cases the arrhythmia is discovered during routine medical examinations. The authors believe, therefore, that physicians must take into consideration this disturbance which is benign but which probably has a definite pathologic cause.

BUNDLE BRANCH BLOCK: A REVIEW OF 100 CASES

ROBERT W. LANGLEY, M.D., JOSEPH C. REED, M.D., AND DAVID C. UTZ, M.D., LOS ANGELES, CALIF.

A study has been made of 100 cases of bundle branch block occurring in a total of 6,900 patients, who received an electrocardiographic examination at the U. S. Naval Hospital, Long Beach, Calif. Only cases demonstrating a QRS duration of 0.2 second or more and indicating in the precordial leads asynchronous activation of the ventricles were selected.

In the survey there were twenty-eight patients under 40 years of age, including seven under 20 years. Twenty-nine patients revealed no apparent organic heart disease as determined by the cardiac history and physical, laboratory, and x-ray examinations. Thirteen of these twenty-nine cases, or 44 per cent of the "no apparent disease" group, were under 40 years of age. Of the group of twenty-nine with no apparent disease, eighteen had a wide "S" wave pattern of bundle branch block; six (33 per cent) of the eighteen were under 40 years of age.

The identification of etiology revealed that the largest single group, thirty-five patients, had coronary heart disease, of which eighteen presented evidence of myocardial infarction. There were eighteen individuals with hypertensive heart disease. The balance of the patients were included in a miscellaneous group consisting of rheumatic, syphilitic, congenital, and infectious heart disease. The two patients who comprised the group of infectious heart disease had mumps and diphtheritic myocarditis; both patients survived.

The classification of the bundle branch block was based upon the multiple precordial leads. There were forty-four cases of right bundle branch block with a delay in the intrinsic deflection presenting an M shaped QRS pattern in the precordial leads over the right side of the heart. Thirty-nine cases had a delay in the intrinsic deflection presenting a M shaped QRS pattern in the precordial leads over the left side of the heart characteristic of left bundle branch block. The remainder of the series was unclassified because the precordial leads from both the lateral sides of the heart were not available. Of the thirty-nine patients with left bundle branch block, eight had a Q wave in the first standard lead, and five of the latter eight had myocardial infarcts.

Six patients, two with no apparent heart disease, have had a known bundle branch block for periods ranging from eight to nineteen years. Four of these have a wide S pattern.

It is concluded that bundle branch block is not uncommon, that it occurs more frequently in the younger age group than was formerly believed, and that many of the individuals with this abnormality present no evidence of organic heart disease. This series supports the present opinion concerning the more favorable prognosis in those patients having the wide S pattern. The generally accepted grave prognosis associated with all types of bundle branch block must be modified in view of the existing cases of block occurring in individuals without apparent heart disease and of the increasing number of cases reported of patients who have heart disease and have had bundle branch block for over ten years.

ELECTROCARDIOGRAPHIC STUDIES IN PUERTO RICO WITH UNIPOLAR PRECORDIAL LEADS IN NORMAL INDIVIDUALS OF BOTH SEXES AND AT DIFFERENT AGES

RAMON M. SUAREZ, M.D., OFFICIAL DELEGATE, PUERTO RICO

The author presents the last of four reports based on the study of the unipolar electrocardiograms made in 161 normal Puerto Rican natives of both sexes between 5 and 46 years of age. Previous communications dealt with T waves as found in precordial leads, pulse frequency, anatomic position of the heart and $\hat{A}_{QRS}$, and the unipolar potentials of the extremities. The present report deals with the results obtained by using the precordial leads in the same group of individuals.

Previous studies of the precordial leads in normal persons have been made on adults and infants. No reports have been found in medical literature on the precordial leads in normal persons from 15 to 18 years of age.

The following are the most important findings: (1) The S-T interval was frequently found to be slightly elevated (not more than 1.5 millimeters). The single instance of S-T depression was recorded in V_6 in a man. (2) The P wave had a duration of as much as 0.12 second in only one woman, in V_3, V_4, and V_5. (3) The P-R interval did not exceed 0.22 second. (4) The duration of the QRS complex was as great as 0.12 second in one man, in V_5, and in one woman, in V_1 and V_2. (5) R-T interval was found between 0.24 and 0.44 second, with an average of 0.32 second. (6) P was of a low voltage in leads taken from the right, and inconspicuous or flattened in leads taken from the left precordium. (7) Q was absent in V_1, V_2, and V_3. (8) The R wave increased in amplitude progressively from V_1 to V_5. In a man the lowest R wave was found in V_1; in a woman, in V_4 and V_5. In both sexes the highest R wave, on an average, was found in V_5. (9) S waves were prominent in V_1, increased in amplitude in V_2, and then diminished in amplitude progressively to V_6. (10) The T wave varied considerably; in children of both sexes, 5 to 11 years of age, this wave may be negative in V_1, V_2, V_3, V_4, and perhaps in V_5; in youngsters and in women, in V_1, V_2, and V_3; and in men only in V_1. (10) A U wave occurred more frequently in adults than in adolescents and children. In all age groups the incidence of U waves was a little more in women than in men.

CONCEALED A-V CONDUCTION: THE EFFECT OF BLOCKED IMPULSES ON THE FORMATION AND CONDUCTION OF SUBSEQUENT IMPULSES

R. LANGENDORF, M.D., MICHAEL REESE HOSPITAL, CHICAGO, ILL.

1. The spread of an impulse which affects the A-V junction by penetrating into it without traversing it, thus failing to reach the auricles or ventricles (depending on the direction in which the impulse travels), finds no direct expression in the electrocardiogram. Indirect evidence of such concealed A-V conduction is the influence of the blocked impulse on the transmission time or on the formation of a subsequent impulse.

2. The literature dealing with the effect of blocked impulses on conduction and formation of subsequent impulses is reviewed. (a) The simplest example of the effect of a blocked impulse is the postextrasystolic P-R prolongation due to blocked retrograde conduction after an interpolated ventricular premature systole. (b) Similarly, the failure of the sinus impulse following a ventricular premature systole to elicit a ventricular response may be due, in some instances, to the inability of the A-V junctional tissues to transmit the impulse

after it has been affected by the blocked retrograde impulse of the ventricular premature systole, and not to refractoriness of the ventricular muscle. (c) The pause after ventricular premature systoles in the presence of auricular fibrillation indicates that a retrograde impulse has affected the junctional tissues. (d) The increase in the grade of a partial A-V block following ventricular premature systoles, even if they are not followed by a retrograde P, demonstrates the effect of blocked retrograde impulses. (e) Cases of complete forward block in the A-V junction and preserved retrograde response show the effect of the blocked forward impulse on subsequent retrograde conduction. (f) A blocked retrograde impulse, by reaching a depressed area in the A-V junction prematurely, may prolong the period of rest in that area and thus shorten the conduction time of the subsequent forward impulse. (g) It is conceivable that in depressed cardiac muscle an impulse, falling into the supernormal phase of a preceding blocked impulse, may be conducted faster instead of being delayed by the effect of the blocked impulse. (h) Multiple blockage may occur as a result of a blocked impulse which was partially conducted and which influenced the subsequent impulse in the same way as a completely conducted one; such a mechanism is probably common in auricular flutter. (i) A blocked A-V nodal premature systole may account for a "dropped beat," and a blocked and interpolated nodal premature systole can give rise to an apparently unexplained P-R prolongation of a single beat. (j) In cases of A-V dissociation some of the impulses of the slower pacemaker (S-A node), after passing and discharging the faster A-V nodal pacemaker, may be stopped below the latter before reaching the ventricles. The result of such concealed A-V conduction is a disturbance in the impulse formation of the nodal pacemaker.

3. Three new instances demonstrating the effect of blocked A-V impulses on succeeding impulse conduction, and one showing the influence on subsequent impulse formation, are reported and illustrated. They demonstrate: (a) the effect of a blocked auricular premature systole on A-V conduction of a subsequent auricular premature systole from the same focus; (b) the effect of the blocked auricular impulses on subsequent A-V conduction in a case of 2:1 A-V block, depending on the exact position of the blocked P wave in the cardiac cycle, thus confirming the existence of a "phase of interference" and explaining the transition from one grade of block to another; (c) the effect of the blocked flutter impulses in a case of auricular flutter with 2:1 A-V conduction giving rise to a pseudo-alternans of A-V conduction; and (d) a hitherto unreported disturbance of impulse formation, that is, discharge of the A-V nodal pacemaker by blocked reciprocal beats.

4. These observations support the view that concealed A-V conduction may account for the difficulty in analyzing some curves of auricular flutter with a varying ratio of A-V conduction. The same phenomenon may also explain some of the discrepancies encountered in the construction of recovery curves of A-V conduction in cases of partial A-V block based on simple correlation of the P-R and R-P intervals.

SINOAURICULAR BLOCK

L. Gonzalez Sabathie, M.D., and Fernando Gaspary, M.D.,
Official Delegates, Argentina

The authors report fifteen cases of proved sinoauricular block and review the evolution of the presently accepted ideas on this subject. They emphasize their agreement with the conclusion of Vidoya, González Videla, and Aguiar. The classification of complete and incomplete block is accepted. Complete sinoauricular block is divided as follows; (1) simple increase in sinoauricular conduc-

tion time, (2) progressive increase with auricular failure, and (3) progressive increase without auricular failure. Complete block may provoke diastolic standstill or shift of the pacemaker to an idioventricular center.

Incomplete block may be of minimal degree and escape detection. Periodic sinus arrhythmia is a frequent form of this type of block, but little has been written on the subject. The authors refer to sinus standstill as sinus abortion, and hold the opinion that this is a true sinoauricular block. An analysis is made of complex forms of sinoauricular block influenced by the activity of secondary centers.

In the cases studied the following causes for a sinoauricular block were recognized; (1) vagotonic state, (2) arteriosclerotic heart disease, and (3) digitalis poisoning. The prognosis and treatment of sinoauricular block is discussed.

ARTERIAL HYPERTENSION—ITS MEDICAL AND SURGICAL ASPECTS

F. Martinez de la Cruz, M.D., and J. Levy Boladeres, M.D., Cuba

1. Renal arteriosclerosis is the first step in the development of elevation of blood pressure. Arterial constriction (renal ischemia, Goldblatt's phenomenon) plays a paramount role in the production of arterial hypertension.

2. Page and co-workers in North America and Houssay in Argentina, have elaborated the theory of an enzyme called renin as a causative agent of arterial hypertension. This substance is normally secreted by the kidneys into the circulatory system. The combination of renin and hypertensinogen (a pseudoglobulin substance formed in the liver), or renin activator as it is also called, produces Page's angiotonin or Houssay's hypertensin. These substances circulating in the blood stream determine arterial constriction and, consequently, arterial hypertension.

3. The existence of a substance called hypertensinase has also been demonstrated by Argentine workers. This is normally produced in the kidneys and its function is to neutralize the hypertensive action of hypertensin. This substance may be responsible for the hypotensive effects of renal extracts.

4. Surgical procedures are useful in a number of cases. Vitamin A, renal extracts, and thiocyanate are the drugs most widely employed at the present time.

5. In 1932, Dr. Domingo H. Gomez Gimeranez of Cuba suggested the existence of a hypotensive and urolytic substance which is normally produced in the cortex of kidneys, and which has been named Nephreptine by the author.

RETINAL ANGIOSCOPY IN ESSENTIAL ARTERIAL HYPERTENSION (A STUDY OF 300 CLINICAL CASES)

M. Puig Solanes, M.D., Active Member, National Institute of Cardiology, Mexico

The pathogenesis, nature, and clinical significance of fundus changes in essential hypertension are still obscure. Clarification was sought by (1) a statistical study of the incidence of retinal changes; (2) their correlation with systemic symptoms; and (3) a correlation of the retinal changes with the data from the general clinical study (arterial tension values, large vessels status, cardiac, and renal function, etc.).

Clinical Material.—Three hundred patients with essential arterial hypertension have been studied. These were chosen at random from a group of 790 patients examined during the last two years at the National Institute of Cardiology.

Method.—The fundus modifications, the systemic changes, and the laboratory data have been tabulated. Statistical studies of the fundus modifications and the modifications of the general state have been made. The percentage and the corrected arithmetical mean with the calculation of the standard deviation and the coefficient of variation were computed in each patient. These quantitative data have been presented in graphic form.

Conclusions.—

1. The two kinds of retinal arterial narrowing in essential hypertension, that is, uniform narrowing and localized constrictions, are probably two different phenomena and not simply two ophthalmoscopic variations of the same phenomenon. This opinion is supported by the failure of both changes to occur frequently in the same eye; by the lack of parallelism in the intensity of the reaction when both co-exist in the same eye; and by the evident relationship of localized constrictions to the diastolic blood pressure, lesions of the retinal parenchyma, and cardiac and renal insufficiency.
2. The evidence indicates that uniform narrowing is a manifestation in the retina of tonic arteriolar contraction of humoral origin, and that localized constriction represents spasm from a superimposed action of the vasomotor nerves.
3. The primary phenomenon in the fundus of hypertensive patients is the tonic contraction of the retinal arterioles. We must recognize, however, that, taking the group of patients as a whole, this contraction is slight and that although it increases when the diastolic pressure rises, it does not bear any direct relationship to it.
4. Uniform narrowing has a proportional relationship to sclerosis of the retinal small arteries, which confirms the opinion that tonic contraction is the pre-existing phenomenon in the ocular circulatory system.
5. Vascular spasm is related to lesions of the retinal parenchyma and to cardiac and renal insufficiency. This confirms its significance as a sign of "activity" and its importance as a prognostic aid.
6. The existence of retinal vascular sclerosis in a hypertensive patient does not imply the existence of aortic sclerosis, but the statistical data show that it may suggest the presence of associated sclerosis of the coronary system.
7. The papilloretinal edematous lesions (edema, cotton-wool patches, detachment of the retina, and choked disc) and the nonedematous lesions (shiny patches) are quantitatively related in our statistics with the degree of cardiac and renal insufficiency. The first type is a manifestation of "activity" or progression of the hypertension, and the second type is a manifestation of an old established process. The identification of one or the other type of involvement indicates in a general way whether the cardiac muscle and the renal parenchyma have been harmed by a rapidly or a slowly developing process.
8. The variations in the caliber, degree of spasm, and amount of sclerosis of the retinal arterioles in hypertensive patients with retinopathy reflect a peripheral circulatory determinant and are not the result of noxious action of supposed toxic products retained by insufficient renal elimination.
9. The author points out that the high values of the standard deviation and the coefficient of variation which frequently accompany the arithmetical mean show how widely scattered are the individual values around the mean. The degree of the fundus changes in hypertensive patients is not always proportional to the clinical state. This reflects the variability in the evolution of the disease. Although Page and Corcoran insist that the ophthalmoscopic examination continues to be the most useful method "to discover the grade and the severity of vascular deterioration in a hypertensive patient," excessive caution is to be used in applying deductions which are valid from a general point of view to every patient.

VALUE OF THE PRESSOR TEST IN HIGH BLOOD PRESSURE

ALBERTO C. TAQUINI, M.D., VICE PRESIDENT, CENTER FOR CARDIOVASCULAR RESEARCH, ARGENTINA

Comparative studies were made in 100 patients with high blood pressure by using the cold pressor test after the technique of Hines and Brown, and the Taquini and Garcia Càmpo test, consisting in the intravenous injection of 0.025 Gm. of efetonine. The patients belonged to types I, II, and III of the classification of Keith, Wagener, and Barker. Ten patients had symptoms of hypertensive heart disease. In six individuals determinations were made of the minute-volume flow with four samples, following the Grollman technique.

In patients belonging to type I, the response to cold varied between 8 and 60 mm. Hg, with an average value of 24.2: Efetonine gave a response of between 16 and 72 mm. Hg, with an average of 31.4. In patients belonging to type II, the response to cold was between 12 and 60 mm. Hg, with an average value of 31; efetonine gave a response between 20 and 80 mm. Hg, with an average of 42.7. In the patients of type III cold gave a response between 20 and 70 mm. Hg, with an average value of 37.8; with efetonine the figures were between 28 and 72 mm., with an average value of 51.4 In ten patients with hypertensive heart disease the highest response to cold was 22 mm. Hg, the lowest was 2 mm. and the average of all the group was 11.7; responses to efetonine were between 8.28 and 22.1 mm. Hg, respectively.

Both tests showed a relationship to the basal blood pressure but not to the maximal variation or the variability of the blood pressure.

The determinations of the minute-volume and the correlated functions during the cold pressor test showed that there was an increase in the use of oxygen of between 6.7 and 33.8 per cent. The minute-volume flow in general was parallel to the oxygen consumption. The difference of the oxygen content in arteries and veins was maintained without significant variation. The studies made with efetonine showed an increase of between 16.5 and 46.1 per cent in the use of oxygen. The minute-volume was also found to be increased between 53.8 and 100.2 per cent. This relatively higher increase of the minute-volume in relation to the use of oxygen was accompanied by a decrease of the arteriovenous oxygen difference varying between 9.6 and 35.4 per cent.

It is concluded that the variations in the minute-volume, the hemodynamic factors caused by a high blood pressure, and the organic changes in the vascular system may explain the differences observed between the cold pressor and efetonine tests. It is pointed out that these factors have to be taken into consideration when deductions concerning the vasomotor reactivity of hypertensive patients are based upon the results of the pressor tests.

THE ROLE OF SURGICAL TREATMENT IN THE MANAGEMENT OF HYPERTENSION

MAX M. PEET, M.D., AND EMIL M. ISBERG, M.D., UNIVERSITY OF MICHIGAN MEDICAL SCHOOL AND HOSPITAL, ANN ARBOR, MICH.

The discovery of hypertension in a patient fixes a responsibility; a chronic disease henceforth must be managed systematically and scientifically. It is necessary to be on the alert for evidences of activity and progression of the hypertensive state. Such manifestations constitute the indication for surgical treatment. Splanchnic resection has proved capable of arresting, and sometimes reversing,

the progressive deterioration of arterial hypertension in a significant percentage of patients. The earlier the evidences of progressive hypertensive disease are recognized and splanchnicectomy is performed, the more likely are the results of surgical treatment to be beneficial.

EXPERIENCES IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS WITH PENICILLIN

ARTHUR J. GEIGER, M.D., YALE UNIVERSITY SCHOOL OF MEDICINE, NEW HAVEN, CONN.

Twenty-two patients with subacute bacterial endocarditis were treated with penicillin given in long courses and in large doses. Cure was achieved in twenty patients (in twelve patients cure has endured from one to two and one-half years thus far). One patient had a return of the disease within two months of treatment, and another patient suffered a reinfection six months after her original cure; both patients were again cured.

The underlying heart disease was congenital in two cases and rheumatic in the others. The patients ranged in age from 3 to 65 years. None of the survivors are invalids.

The infection was due to *Streptococcus viridans* in each case. The penicillin resistance of the infecting organism ranged from 0.01 to 0.05 units per cubic centimeter of culture required to inhibit growth in vitro.

Four methods of penicillin administration were tested: (1) intramuscular injections at two-hour intervals, (2) continuous intramuscular infusion-drip, (3) continuous intravenous infusion-drip, and (4) one or two daily intramuscular deposits of massive doses of penicillin in an oil and beewax medium. Serum penicillin concentrations with each mode of treatment indicated the superiority of the continuous intravenous and of the intramuscular deposit (in oil and beewax) methods for maintaining sustained penicillin concentration in the blood.

The total amounts of penicillin administered in the cured patients ranged from 3,900,000 to 102,000,000 units, and the duration of treatment ranged from three weeks to seventeen months.

In one cured patient, who died nine months later of another disease, the fibrocalcific, sterile, and abacterial lesion of the previous endocarditis which was seen at necropsy proved anatomically that the infection had been eradicated.

Representative cases were presented briefly and were illustrated by projected charts.

PENICILLIN IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS: FURTHER STUDIES IN TWENTY-ONE PATIENTS

FLAVIO JIMENES ROMO, M.D., ACTIVE MEMBER, NATIONAL INSTITUTE OF CARDIOLOGY, MEXICO

The author reports the results of treatment of twenty-one patients with subacute bacterial endocarditis by the use of penicillin. The patients were divided into two groups according to the methods of treatment as follows: the first group included nine individuals who were treated by different physicians, using different methods of administration of the drug; the second group was composed of twelve patients whom the author treated according to a relatively uniform method.

The time of evolution of the disease, the general state of the patient, and sensitivity of the isolated streptococcus to penicillin were alike in both groups.

Penicillin was administered to all patients by the fractionated intravascular method; injections were given at first every three hours and later every two hours. The author stresses that the aim of any method, regardless of the particular procedure employed, is to maintain the highest penicillin blood levels.

The first group of patients received from 160,000 to 240,000 Oxford units of penicillin, the second group received from 160,000 up to 2,000,000 Oxford units daily. The average total dose was 11.5 million units in the first group and 22.5 million units in the second group of patients. Treatment was given over a period of six to seven weeks; heparin was used in three cases of the first group and in none in the second. Other therapeutic measures (iron, vitamins, blood transfusions, etc.) were used in the patients of both groups.

The following results were obtained: In the first group eight patients died and one was cured (11.1 per cent cured); in the second group there were four deaths and eight cures (66.6 per cent of the cases were cured).

These figures stress the necessity of employing high doses of penicillin. It is to be expected that the author's statistics will give better results in the future since he now systematically employs large doses of penicillin, 1.2 million units daily with a total dose of 50 million units per patient.

PULMONARY EMBOLISM IN MEDICAL PATIENTS: A COMPARISON OF INCIDENCE, DIAGNOSIS, AND THE EFFECTS OF TREATMENT OF 273 CASES AT THE MASSACHUSETTS GENERAL HOSPITAL IN TWO FIVE-YEAR PERIODS (1936 TO 1940 AND 1941 TO 1945 INCLUSIVE)

JACQUES CARLOTTI, M.D.,* IRAD B. HARDY, JR., M.D., ROBERT R. LINTON, M.D., AND PAUL D. WHITE, M.D., MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

An analysis has been made of the incidence, symptoms and signs, and treatment of pulmonary embolism in medical patients at the Massachusetts General Hospital during two five-year periods, from 1936 to 1940 inclusive (Group A) and from 1941 through 1945 (Group B). During the entire ten years the ratio of patients with pulmonary embolism on the medical wards (0.6 per cent) was more than twice that of patients on the surgical wards (0.24 per cent). Although there were actually more than twice as many surgical cases (98,642) as medical (45,523), more than half (53.4 per cent) of all the patients with pulmonary embolism were medical (273 as compared to 238 surgical). Of the 273 medical cases with pulmonary embolism, 122 were diagnosed during the first five years and 151 during the second, due at least in part to an improvement in diagnostic ability.

Males predominated, making up 56.5 per cent in Group A and 60.3 per cent in Group B. The great majority of the patients were over 40 years of age (83.8 per cent) and over one-half were from 50 to 70 years of age. The majority of the patients had cardiac disease (59 per cent in Group A and 70.8 per cent in Group B). All kinds of heart disease were represented, especially the rheumatic, hypertensive, and coronary forms. Congestive failure was frequent as a background and auricular fibrillation was present in nearly one-third of the patients.

Of the symptoms, chest (mostly pleural) pain was the most common but not the earliest, being found in about one-half the patients (49.1 and 56.9 per cent in the two groups cited). Dyspnea was present in one-third (31.9 and 35.7 per cent), but hemoptysis occurred in a relatively small group (10.4 and 18.5 per cent). Tachycardia out of proportion to the degree of fever or dyspnea was a

*French Government Research Fellow in Medicine.

prominent sign. Physical abnormalities in the chest were often absent; a pleural friction rub was found in less than 10 per cent of the patients (9.8 and 8.6 per cent). The roentgenologic diagnosis of pulmonary infarction improved considerably in the second five-year period as compared with that in the first (57 and 33 per cent). The electrocardiographic pattern of acute cor pulmonale was evident in about one-fifth of the patients electrocardiographed.

Autopsies in ninety (72 per cent) of the 125 patients who died showed massive embolism in 50 per cent. In only a few cases (twelve) were thrombi found in the right heart chambers. Over 75 per cent of those whose leg veins were examined showed thrombosis therein.

In only one patient during the first five-year period were the femoral veins interrupted, but in the second period the operation was done bilaterally on either the superficial or common femoral veins (the latter are the preferable site) in sixty patients with a reduction of early mortality (within one month) to 28.3 per cent as compared with 50.7 per cent in those without operation.

The possibility of pulmonary embolism in medical patients, especially in those with cardiac disease, should be constantly borne in mind and treated prophylactically by bilateral common femoral vein interruption when discovered.

CARDIAC ASTHMA AND ACUTE EDEMA OF THE LUNGS IN MITRAL STENOSIS WITH AURICULAR FIBRILLATION

ISAAC BERCONSKY, M.D., AND J. NEUMAN, M.D., ACTIVE MEMBERS, ARGENTINA

The authors studied fifty-one patients with mitral stenosis or mitral disease with paroxysmal dyspnea In twenty-one (two with arterial hypertension and five with aortic valvular disease) the rhythm was of sinus origin. In eight of the thirteen patients with auricular fibrillation and normal blood pressure, the abnormal auricular rhythm existed before the onset of cardiac asthma and acute edema of the lung. Thus, acute auricular insufficiency was not the cause of these pulmonary phenomena in these patients.

The more probable factors determining the sudden pulmonary stasis in mitral stenosis with or without auricular fibrillation appear to be (1) shortening of diastolic filling time of the ventricles and decrease in circulation to the ventricular muscle itself originated by tachycardia and (2) greater relative obstruction of the mitral orifice caused by an increased venous return to the heart.

MORPHINE TREATMENT OF ACUTE PULMONARY EDEMA

L. GONZALEZ SABATHIE, M.D., OFFICIAL DELEGATE, ARGENTINA

The author believes that morphine or any similar alkaloid given by intravenous injection is very effective in the treatment of acute edema of the lungs. He has used it in fifty patients with acute edema of the lungs in doses of 1 or 2 centigrams. A favorable response was apparent in from two to five minutes after the injection; usually within approximately ten minutes the patient had practically recovered. No undesirable effects were noted. In some patients the extremities were bandaged. All patients received additional medication, but none were bled. The author points out that this method of therapy should be applied only in those patients who have crepitant râles and hemorrhagic sputum; he warns that if the pulmonary asphyxia and the dyspnea is of central nervous system origin, morphine must not be used.

HEART DISEASE AND PREGNANCY

CH. LAUBRY, M.D., AND D. ROUTIER, M.D., HONORARY MEMBERS, FRANCE

The rheumatic cardiovalvular disorders are almost the only ones to be considered here, since the age of the pregnant patient makes exceptional the occurrence of congenital as well as arterial or hypertensive heart disease.

There are three factors to be analyzed in connection with the tolerance of the pregnant woman to heart affections: (1) the mechanical factor inherent in the valvular lesion; (2) the factor of progressive development, inherent in the inflammatory process which causes the lesion; (3) the endocrine factor related to pregnancy. The factor of evolution is the most important of all three since the majority of pregnant heart patients requesting medical care have mitral stenosis (75 per cent in our statistics), which is the most progressive form of rheumatic lesion of the heart. It is, therefore, essential to understand clearly what decisions may have to be made in a pregnant patient with mitral stenosis. The prognosis depends upon the establishment of the diagnosis, and upon whether the rheumatic heart affection remains stationary or progresses. It should be recognized, however, that some patients with mitral disease present signs of activity of the rheumatic disease after delivery. It is important, therefore, to watch these patients before and after delivery and to eliminate, as far as possible, everything that may reactivate the rheumatic state.

All acute accidents occurring in patients with mitral stenosis are formal indications for interruption of pregnancy. These include the onset of auricular fibrillation, hemoptysis, acute edema of the lungs, and hemiparesis. It is necessary to remember that previous successful pregnancies do not guarantee the favorable outcome of a given pregnancy, because the involvement may have progressed since the previous pregnancy.

For the interruption of pregnancy, surgical methods rather than medical methods are advised; embolic accidents are thereby reduced. Whenever interruption of pregnancy is indicated in a patient with mitral stenosis, sterilization is clearly in order.

INTERMITTENT VENTRICULAR TACHYCARDIA IN YOUTH. REPORT OF CASE WITH FATAL TERMINATION

KEMPSON MADDOX, M.D., SYDNEY, AUSTRALIA

Instances where young people exhibited paroxysms of ventricular tachycardia, lasting a few seconds to a few minutes, separated by periods of normal rhythm or extrasystoles of the same type as those constituting the paroxysms, were described in 1927 by Gallavardin and Veil, as *tachycardic en salves*. Wilson and associates and Anderson reported on patients with similar conditions in 1931 and 1932. There were no signs of heart disease present, and the irregularity was generally considered to carry a good prognosis. Other cases have been reported, but the total number is not large.

That the prognosis under such circumstances is not necessarily always favorable is suggested by the following case report:

E. M., a male medical officer, 26 years of age, was found dead in his tent during the Borneo campaign of 1945. He had appeared to be perfectly well immediately before. No autopsy was performed.

This medical officer had presented himself to me in 1937, as an example of cardiac arrhythmia for presentation to his fellow medical students. He had played football strenuously throughout the whole of his school and undergraduate

career, without any undue distress, fatigue, or palpitation. Physical examination revealed a grossly irregular heart beat, no clinical cardiac enlargement, and no thrills or murmurs in any area. The arteries seemed normal. Blood pressure was 125/95. The chaotic heart action was uninfluenced by exercise, atropine, or carotid sinus stimulation. He was a nonsmoker. Standard limb lead electrocardiograms revealed a basic sinus arrhythmia (P-R interval 0.12 second), interrupted by (1) frequent right ventricular extrasystoles, often coupled, followed by pauses of variable length; (2) short salvos of ventricular tachycardia, slightly irregular in rhythm, commencing prematurely and followed by regular compensatory pauses. The number of complexes per paroxysm usually varied between six and nine. The sinus complexes were not remarkable, apart from a high voltage. Their form gave no indication of the presence of coronary disease. Unfortunately, no precordial leads were obtained.

X-ray study revealed a slight increase in transverse diameter corresponding to the "athletic heart." The past medical history was entirely uneventful. The irregularity had been noted at the age of 3 years and had been considered to be due to multiple extrasystoles and of no significance. There had been no complaints referable to the cardiovascular system during the remainder of his medical course or internship. He was at first rejected for naval or military service, but because of his fine physique and physical record, he was ultimately accepted and sent overseas.

The value of quinidine was suggested to him when the true nature of the irregularity was first recognized, but it was later discovered that he had never followed this advice. Whether quinidine plus avoidance of battle strain in the tropics whould have lengthened his life is purely speculative. It is not proved but is less speculative to assume that his death was due to ventricular fibrillation or standstill.

This patient is reported on to redirect attention to a rare form of intermittent ventricular tachycardia which is unassociated with signs of organic heart disease, and which may be termed the "Gallavardin" type. This disturbance may begin in infancy and may occasionally terminate in sudden death in the absence of the protective effects of quinidine.

THE TREATMENT OF CONGESTIVE HEART FAILURE

MAHLON C. COOLEY, M.D., LOS ANGELES, CALIF.

Treatment of congestive heart failure has not changed much in ten years, but as we now better understand the disease and comprehend more fully methods of treatment, we apply treatment to the disease unhesitantly and with definite expectancy.

Rest is being studied as a definite remedy requiring a dosage to meet the particular need of an individual patient. No longer is there insistence upon a particular kind of rest (bed, chair, recumbent, and sitting). The criterion is rest of the heart muscle, thus saving the optimum number of heart beats consistent with the heart functioning as a good pump and a rhythmic one.

The sedative armamentarium is without recent change.

Morphine is still the drug of choice in the majority of cases. The contraindications are few but important. Due caution should be observed. In certain psychoneurotic complications, the exhibition of appropriate doses of phenobarbital, sodium bromide, or chloral hydrate is worthy of consideration.

Digitalis is yet the drug of choice, because it is the only drug which, by its triple action on nerve, conducting tissue, and muscle, reverses the state, slows the heart, regulates the rhythm and strengthens the contraction, and results in the

optimum: a better pump, a rhythmic pump, and a more rested one. Powdered leaf is evidently the most used preparation with certain pure glycosides gaining rapidly in favor. Tincture of digitalis for apparent good reason is being used less and less frequently. Cedilanid is the most potent of the glycosides but should be reserved for emergencies and for those patients in whom oral administration is impossible. Digitoxin is the preparation which merits the favor it is rapidly gaining. It has many advantages over digitalis leaf: injectability, stability, and accurate dosage. The prophesy that digitoxin will replace digitalis in a few years is not without supporting evidence.

The relation of salt restriction to the solution of the difficult problem of edema has claimed much attention in recent months. Without any doubt, thorough and proper handling of salt restriction, that is, restricting salt to a minimum through the aid of proper diet instruction, is a notable advance in cardiac therapeutics. Not only is there a lessening of ventricular strain, but the patient is rendered happier by being able to quench a normal thirst as well as prevent dehydration.

The following papers read before the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946, will be published in a later issue of the JOURNAL:

Weight of the Red Blood Corpuscles in Heart Failure Determined With Labelled Erythrocytes During and After Decompensation. G. Nylin, M.D., and S. Hedlund, M.D., Stockholm, Sweden.

Circulatory Adaptations in Ayerza's Syndrome—Black Cardiacs. Alberto C. Taquini, M.D., J. C. Fasciolo, M.D., J. R. E. Suarez, M.D., and H. Chiodi, M.D., Buenos Aires, Argentina.

The Diagnosis of Tricuspid Valve Disease. Salvador Aceves and Rafael Carral, Mexico, D. F., Mexico.

Comparative Study of the Intracavity Potential in Man and in Dog. Demetrio Sodi Pallares, M.D., Mario Vizcaino, M.D., Jorge Soberón, M.D., and Enrique Cabrera, M.D., Mexico, D. F., Mexico.

American Heart Association, Inc.

1790 Broadway, New York 19, N. Y.

Telephone Circle 5-8000

PROGRAM OF THE ANNUAL MEETING AND TWENTIETH SCIENTIFIC MEETING OF THE AMERICAN HEART ASSOCIATION, INC.

To Be Held at the Hotel President, Atlantic City, N. J., June 6 and 7, 1947

ANNUAL MEETING

This important meeting, as well as a meeting of the representatives of local heart associations will be held in the Ballroom of the Hotel President beginning at 9:00 A.M., June 6, 1947.

ANNUAL DINNER

This will be held in the Ballroom of the Hotel President at 7:30 P.M., June 7, 1947. "Top Nazis" will be the subject of a talk by Colonel Ellis C. Vander Pyl. Colonel Vander Pyl, of Chief Operations Section, War Crimes Branch, United States Army, was for many months in close contact with top-ranking Nazis during war trials in Nürnberg. He will relate his associations with Goering, Hess, and the entire coterie who made world headlines. The toastmaster will be Dr. Howard F. West. Dress will be informal.

SCIENTIFIC MEETING*

The program for the three scientific sessions has been prepared by the following committee:

J. M. Askey, M.D., Los Angeles
Emmet B. Bay, M.D., Chicago
Herrman L. Blumgart, M. D., Boston
George E. Burch, M.D., New Orleans
Ignacio Chávez, M.D., Mexico City
Douglas Deeds, M.D., Denver
Arthur C. DeGraff, M.D., New York
Norman E. Freeman, M.D., San Francisco
Franklin Johnston, M.D., Ann Arbor
John D. Keith, M.D., Toronto
Robert L. King, M.D., Seattle
Chester M. Kurtz, M.D., Madison
William B. Kountz, M.D., St. Louis
E. Sterling Nichol, M.D., Miami
Irvine H. Page, M.D., Cleveland
William B. Porter, M.D., Richmond
Ramon M. Suárez, M.D., Santurce, P. R.
Helen B. Taussig, M.D., Baltimore
J. Ross Veal, M.D., Washington, D. C.
Merritt B. Whitten, M.D., Dallas
Francis C. Wood, M.D., Philadelphia
Edgar V. Allen, M.D., Rochester, Minn. (*Chairman*)

First Scientific Meeting, 2 P.M., June 6, Ballroom, Hotel President

Chairman, Howard F. West, M.D., President, American Heart Association; Secretary, Howard B. Sprague, M.D.

1. The Immediate Electrocardiographic Effects of Circumscribed Myocardial Injuries; An Experimental Study.
   Raymond D. Pruitt, M.D., Rochester, Minn., and Fernando Valencia, M.D., Ann Arbor, Mich.
   Discussion to be opened by Harold J. Stewart, M.D., New York. William Dressler, M.D., New York, and A. M. Master, M.D., New York.
2. The Varied Clinical Syndromes Produced by Dissecting Aneurysm.
   Samuel Baer, M.D., and Harold L. Goldburgh, M.D., Philadelphia.
   Discussion to be opened by William B. Kountz, M.D., St. Louis.
3. Physiologic Studies in Congenital Heart Disease.
   Richard J. Bing, Leroy D. Vandam, and Frank D. Gray, Jr., Baltimore.
   Discussion to be opened by Raymond S. Megibow, M. D., New York.
4. The Effect of Occlusive Arterial Diseases of the Extremities on the Blood Supply of Nerves.
   Joseph T. Roberts, M.D., Washington, D. C.
   Discussion to be opened by Norman E. Freeman, M.D., San Francisco, and Meyer Naide, M.D., Philadelphia.
5. Studies on the Collateral Circulation of Hearts With Acute Coronary Occlusion.
   Myron Prinzmetal, M.D., Los Angeles.
   Discussion to be opened by Herrman L. Blumgart, M.D., Boston.
6. Changes in the Coronary Arteries of Dogs Following Injections of Allylamine.
   L. L. Waters, M.D., New Haven.
   Discussion to be opened by Irving Greenfield, M.D., Woodmere, N. Y.
7. The Effect of Local Compression Upon Blood Flow in the Extremities of Man.
   Robert W. Wilkins, M.D., M. H. Halperin, M.D., and C. K. Friedland, M.D., Boston.
   Discussion to be opened by Geza de Takats, M.D., Chicago.

***Essayists, except the George Brown Memorial Lecturers, will be restricted to a maximum of fifteen minutes. Each must leave a completed manuscript with the secretary for consideration for publication in the American Heart Journal. Each prospective discussor will indicate his wishes in a notation including name, address, and presentation to be discussed which will be handed to the secretary. Each discussion will be from the rostrum and may not exceed three minutes. Questions lacking general interest should be directed to essayists privately after discussion has been completed.**

Second Meeting, 9:00 A.M., June 7

Chairman, J. Ross Veal, M.D., Chairman Section on Peripheral Vascular Diseases; Secretary, Grace Roth, Ph.D.

8. The Functional Pathology of Experimental Trench Foot.
Kurt Lange, M.D., David Weiner, M.D., and Linn J. Boyd, M.D., New York.

9. *The George Brown Memorial Lecture:*
A Consideration of Approximately Four Hundred Patients With Pulmonary Stenosis or Atresia Who Were Treated by Surgical Means.
Helen B. Taussig, M.D., and Alfred Blalock, M.D., Baltimore.

10. Relief of Cardiac Pain by Local Block of Somatic Trigger Areas.
H. Seymour Rinzler, M.D., and Janet Travel, M.D., New York.
Discussion to be opened by David Davis, M.D., Boston, and Maurice S. Jacobs, M.D., Philadelphia.

11. Combined Heparin-Dicumarol Therapy of Myocardial Infarction.
Helen I. Glueck, M.D., Victor Strauss, M.D., and Johnson McGuire, M.D., Cincinnati.
Discussion to be opened by E. Sterling Nichol, M.D., Miami, Irving S. Wright, M.D., New York, and Nelson W. Barker, M.D., Rochester, Minn.

12. The Experience of Rheumatic Patients Who Served in the Armed Forces.
May G. Wilson and Joan W. Payson, New York.
Discussion to be opened by Leo M. Taran, M.D., New York, Benedict F. Massell, M.D., Boston, and George C. Griffith, M.D., Pasadena.

13. The Determination of the Prognosis of Pregnancy in Rheumatic Heart Disease.
Joseph J. Bunim, M.D., and Jeanette Rubricius, M.D., New York.
Discussion to be opened by John J. Sampson, M.D., San Francisco.

Third Meeting, 2:00 P.M., June 7

14. Newer Concept of Stokes-Adams Syndrome.
Sidney Schnur, M.D., Houston.
Discussion to be opened by Stanford Wessler, M.D., Boston.

15. Electrocardiographic Analysis of Cases of Right Axis Deviation.
Charles E. Kossman, M.D., New York.
Discussion to be opened by Harry Vesell, M.D., New York, Stephen R. Elek, M.D., Los Angeles, and H. R. Miller, M.D., New York.

16. Studies in Fluorocardiography.
A. A. Luisada, M.D., F. G. Fleischner, M.D., and M. B. Rappaport, M.D., Boston.
Discussion to be opened by George F. Ellinger, M.D., Philadelphia, and Marcy L. Sussman, New York.

17. The Present Status of Venography in Venous Thrombosis.
Hugh H. Hussey, M.D., and J. Ross Veal, M.D., Washington, D. C.
Discussion to be opened by Edward A. Edwards, M.D., Boston.

18. Night Cramps in Human Extremities.
Harold K. Moss, M.D., and Louis G. Herrmann, M.D., Cincinnati.
Discussion to be opened by Ferdinand R. Schemm, M.D., Great Falls, Mont., and Emil M. Isberg, M.D., Miami Beach.

QUESTIONS AND ANSWERS PERIODS

The American Heart Association With the American Medical Association
(The place of these meetings will be announced.)

Monday, June 9

9:00–11:00 A.M. The Use of Anticoagulants in Cardiovascular Diseases.
N. W. Barker, M.D., Irving S. Wright, M.D., and E. Sterling Nichol, M.D.

2:00– 4:00 P.M. The Diagnosis of Congenital Cardiovascular Diseases.
Herrman L. Blumgart, M.D., Helen B. Taussig, M.D., and Eugene Eppinger, M.D.

Tuesday, June 10

9:00–11:00 A.M. The Peripheral Arterial Diseases.
Irving S. Wright, M.D., and N. W. Barker, M.D.

2:00– 4:00 P.M. The Use of Drugs in Heart Diseases.
Arthur C. DeGraff, M.D., Harry Gold, M.D., and Howard B. Sprague, M.D.

Wednesday, June 11

9:00–11:00 A.M. Hypertension.
I. H. Page, M.D., M. H. Barker, M.D., and J. Q. Griffith, M.D.

2:00– 4:00 P.M. Rheumatic Fever.
R. Duckett Jones, M.D., May G. Wilson, M.D., and George C. Griffith, M.D.

Thursday, June 12

9:00–11:00 A.M. Surgical Treatment for Vascular Diseases.
Norman E. Freeman, M.D., Geza de Takats, M.D., and J. Ross Veal, M.D.

2:00– 4:00 P.M. Problems in Electrocardiography.
Charles T. Wolferth, M.D., Franklin Johnston, M.D., and George Burch, M.D.

Friday, June 13

9:00–11:00 A.M. Management of the Failing Heart.
Francis C. Wood, M.D., Graham Asher, M.D., and James V. Warren, M.D

THE American Heart Association was founded in 1924 "for the study of and the dissemination and application of knowledge concerning the causes, treatment and prevention of heart disease; the gathering of information on heart disease; the development and application of measures that would prevent heart disease; seeking and provision of occupations suitable for heart disease patients; the promotion of the establishment of special dispensary classes for heart disease patients; the extension of opportunities for adequate care of cardiac convalescents; the promotion of permanent institutional care for such cardiac patients as are hopelessly incapacitated from self-support; and the encouragement and establishment of local associations with similar objects throughout the United States."

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The American Council on Rheumatic Fever, organized in 1944, consists of a group of representatives of all national medical organizations concerned with rheumatic fever. It operates administratively through the American Heart Association and carries out the program of the American Heart Association insofar as that relates to rheumatic fever.

Annual membership in the American Heart Association is $2.50 and includes twelve issues of *Modern Concepts of Cardiovascular Disease;* Journal membership is $10.00 and includes a year's subscription to the AMERICAN HEART JOURNAL (January-December), twelve issues of *Modern Concepts of Cardiovascular Disease,* and annual membership in the Association. Contributing membership starts at $25.00 per year; patron membership is $50.00 and over per year. Membership blanks will be sent upon request.

The Association earnestly solicits your support and suggestions for its work. Donations will be gratefully received and promptly acknowledged.